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ORGANIC SYNTHESSES

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AN ANNUAL PUBLICATION OF SATISFACTORY
METHODS FOR THE PREPARATION
OF ORGANIC CHEMICALS

VOLUME 32

1952

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NOMENCLATURE

Preparations appear in the alphabetical order of common names of the compounds. For convenience in surveying the literature concerning any preparation through *Chemical Abstracts* subject indexes, the *Chemical Abstracts* indexing name for each compound is given as a subtitle if it differs from the common name used as the title.

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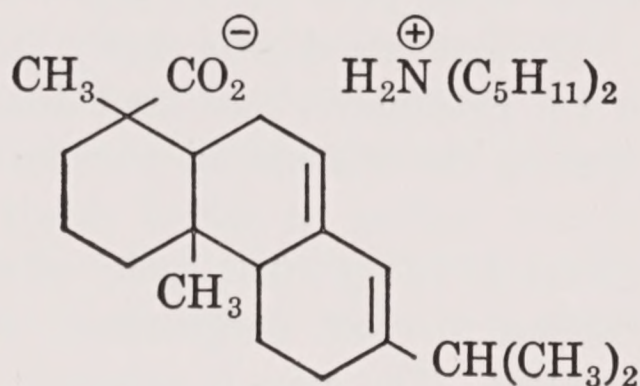
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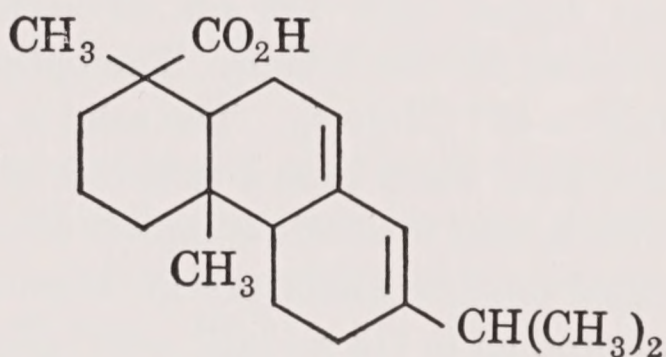
ABIETIC ACID

Wood rosin + HCl → Isomerized wood rosin

Isomerized wood rosin + $(C_5H_{11})_2NH \rightarrow$



Amine salt + CH₃CO₂H →



Submitted by G. C. HARRIS and T. F. SANDERSON.¹
 Checked by R. T. ARNOLD and K. L. LINDSAY.

1. Procedure

Into a 2-l. round-bottomed flask fitted with a 35-cm. reflux condenser are placed 250 g. (0.74 mole) of N-grade wood rosin (Note 1), 740 ml. of 95% ethanol, and 42 ml. of hydrochloric acid (sp. gr. 1.19). A stream of carbon dioxide is passed over the surface of the solution by means of a glass tube which extends downward through the condenser during this reaction (Note 2). The mixture is boiled under reflux for 2 hours (Note 3). At the

end of this time, the ethanol and acid are removed by steam distillation and the water is decanted. The residue is cooled to room temperature and dissolved in 1 l. of ether. The ether solution is extracted with water and dried over 200 g. of anhydrous sodium sulfate. The bulk of the ether is evaporated on the steam bath, and the last traces are removed by fusing the rosin over a free flame and under a vacuum furnished by a water aspirator. The molten rosin, blanketed continuously with carbon dioxide, is most conveniently handled by being poured into a paper boat; yield 245 g.; $[\alpha]_D^{24} -35^\circ$ (Note 4).

The isomerized rosin, 245 g. (0.72 mole) (Note 1), is placed in a 1-l. Erlenmeyer flask and dissolved in 375 ml. of acetone by heating the mixture on a steam bath. To this solution, at incipient boiling, is added slowly and with vigorous agitation (Note 5) 127 g. (0.81 mole) of diamylamine² (Note 6). Upon cooling to room temperature, crystals appear in the form of rosettes. The mass is agitated, cooled well in an ice bath, and filtered by suction. The crystalline salt is washed on a Büchner funnel with 150 ml. of acetone and dried in a vacuum oven at 50° for 1 hour. The optical rotation of this material is $[\alpha]_D^{24} -18^\circ$ (Note 4). The solid is recrystallized four times from acetone. Each time a sufficient quantity (20 ml. per g.) of acetone is used to obtain complete solution, and the solvent is evaporated until incipient precipitation of the salt occurs. The yield of product is 118 g.; $[\alpha]_D^{24} -60^\circ$ (Note 4). An additional 29 g. of product, having the same rotation, can be recovered from filtrates of the previous crystallizations.

The amine salt (147 g.) is placed in a 4-l. Erlenmeyer flask and dissolved in 1 l. of 95% ethanol by heating the mixture on a steam bath. To the solution, which has been cooled to room temperature (Note 7), is added 39 g. (35.8 ml.) of glacial acetic acid, and the solution is stirred. Water (900 ml.) is added cautiously at first and with vigorous agitation until crystals of abietic acid begin to appear; the remainder of the water is then added more rapidly. The abietic acid is collected on a Büchner funnel (Note 8) and washed with water until the acetic acid has been removed completely as indicated by tests with indicator

paper. Recrystallization can be effected by dissolving the crude product in 700 ml. of 95% ethanol, adding 600 ml. of water as described above, and cooling the solution. The yield of abietic acid is 98 g. (40% based on the weight of isomerized rosin; $[\alpha]_D^{24} -106^\circ$ (Notes 4 and 9). The ultraviolet absorption spectrum shows a maximum at 241 $m\mu$; $\alpha = 77.0$ (Note 10).

2. Notes

1. The calculation of molar quantities is based on an acid number of 166 for N-grade wood rosin as obtained from Hercules Powder Company, Wilmington, Delaware. Acid number is the number of milligrams of potassium hydroxide required to neutralize 1 g. of sample.

2. Blanketing the rosin in solution or in the molten state with carbon dioxide serves to keep it out of contact with air to avoid oxidation.

3. The maximum negative optical rotation, $[\alpha]_D^{24} -35^\circ$, is obtained with a minimum reflux time of 2 hours.

4. Rotations are reported as those of 1% solutions in absolute ethanol.

5. The addition of the amine to the hot solution is necessary for the formation of the salt. However, it must be done slowly and with rapid stirring because of the resulting vigorous exothermic reaction.

6. Commercial diamylamine, a mixture of isomers, purchased from Sharples Chemicals Company, Philadelphia, Pennsylvania, was employed.

7. The acid is added to a cooled solution of the salt in ethanol to minimize the chance for isomerization of the liberated abietic acid.

8. An early filtration is desirable for the purpose of removing the abietic acid from the acidic solution where isomerization can take place. Washing with a large volume of water and recrystallizing assures the complete removal of acetic acid.

9. The pure acid is dried in a vacuum desiccator over sodium hydroxide or calcium sulfate, and stored in an oxygen-free atmos-

phere. Undue exposure to higher temperatures will result in isomerization, and contact with oxygen will result in oxidation.

10. The absorption spectrum data were obtained from measurements made with a Beckman Ultraviolet Spectrophotometer. The formulas employed in making the calculations use the term α , specific absorption coefficient.

$$\alpha = \frac{\log_{10} I_0/I}{cl}$$

where I_0 = intensity of radiation transmitted by the solvent; I = intensity of radiation transmitted by the solution; c = concentration of solute in grams per liter; l = length in centimeters of solution through which the radiation passes.

3. Methods of Preparation

Abietic acid has usually been prepared ² from rosin through the acid sodium salt ($3C_{20}H_{30}O_2 \cdot C_{19}H_{29}COONa$) with the subsequent formation and recrystallization of the diamylamine salt. The acid is regenerated from the pure salt by decomposition of the latter with a weak acid such as acetic acid.

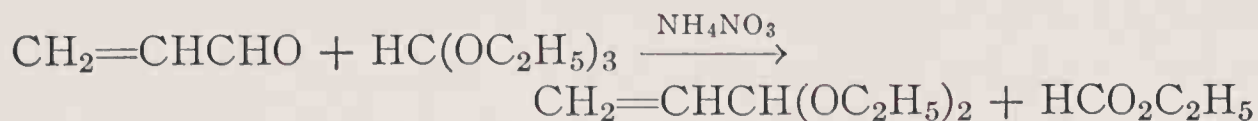
Two improvements have been introduced by the method described above: (1) the abietic acid content of the rosin is increased by acid isomerization, and (2) a much better recovery of acid is obtained by applying the amine salt technique directly to the isomerized rosin, thus eliminating the step involving the acid sodium salt.

¹ Hercules Powder Company, Wilmington, Delaware.

² Palkin and Harris, *J. Am. Chem. Soc.*, **56**, 1935 (1934).

ACROLEIN ACETAL

(Acrolein diethyl acetal)

Submitted by J. A. VANALLAN.¹

Checked by T. L. CAIRNS and R. E. BENSON.

1. Procedure

A warm solution of 3 g. of ammonium nitrate in 50 ml. of anhydrous ethanol is added to a mixture of 44 g. (52.4 ml., 0.79 mole) of acrolein and 144 g. (160 ml., 0.97 mole) of ethyl orthoformate, and the mixture is allowed to react at room temperature for 6–8 hours (Note 1). The light-red solution is filtered, 4 g. of sodium carbonate is added, and the reaction mixture is distilled from the sodium carbonate through a good column (Note 2). The fraction boiling at 120–125° is acrolein acetal and weighs 73–81 g. (72–80%); n_D^{25} 1.398–1.407 (Note 3).

2. Notes

1. Refluxing causes the formation of some resinous material. The solution remains warm for about 1.5 hours after mixing.

2. The column described by Pingert² is suggested.

3. This reaction appears to be of general application; crotonaldehyde diethyl acetal is formed in 68% yield; b.p. 145–147°; n_D^{25} 1.409. (In this preparation the amount of ethyl orthoformate used is reduced to exactly one equivalent since it distils at 142–143°. For this particular acetal, it is preferable to use ethyl orthosilicate according to Helferich.³) Tiglylaldehyde diethyl acetal is formed in 79% yield; b.p. 158–160°; n_D^{25} 1.419.

3. Methods of Preparation

These have been reviewed previously.^{2,4} The procedure described above is an adaptation of a method reported in a German patent.⁵ It has been claimed that the reaction of acrolein with ethanol in the presence of hydrochloric acid² produces a mixture of substances from which no acrolein acetal can be isolated.⁶

¹ Eastman Kodak Company, Rochester, New York.

² *Org. Syntheses*, **25**, 1 (1945).

³ Helferich, Ger. pat. 404,256 (1924) [*Frđl.*, **14**, 228 (1921-1925)].

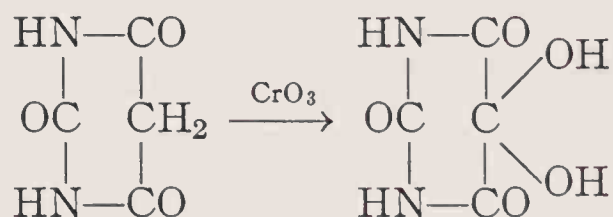
⁴ *Org. Syntheses Coll. Vol. 2*, 17 (1943).

⁵ Schmidt, Ger. pat. 553,177 (1932) [*Frđl.*, **19**, 229 (1932)].

⁶ Hall and Stern, *Chemistry & Industry*, **1950**, 775.

ALLOXAN MONOHYDRATE

(5,5-Dihydroxybarbituric acid)



Submitted by A. V. HOLMGREN and WILHELM WENNER.¹

Checked by T. L. CAIRNS and R. W. UPSON.

1. Procedure

In a 2-l. three-necked, round-bottomed flask with glass joints are placed 850 g. of commercial glacial acetic acid and 100 ml. of water. The flask is fitted with a stirrer. One of the side necks carries a reflux condenser and a thermometer reaching to the bottom of the flask; the other is provided with a stopper which can be replaced by a powder funnel. The flask is surrounded by a water bath. At room temperature 156 g. (1.53 moles) of 98-99% chromium trioxide (Note 1) is added, and the mixture is stirred for about 15 minutes to effect solution of the oxidizing agent.

One hundred and twenty-eight grams (1 mole) of barbituric acid is added in the course of about 25 minutes in portions approximating 15–20 g. The temperature of the mixture rises from about 25–30° at the beginning of the reaction to 50° and is held at that value until all the barbituric acid has been added (Note 2). During the addition, alloxan monohydrate begins to crystallize. The temperature of the solution is held at 50° for 25–30 minutes after completion of the addition of barbituric acid. Then the reaction slurry, which contains the major amount of alloxan monohydrate in crystalline form, is cooled to 5–10° and filtered through a 5-in. Büchner funnel fitted with a piece of filter cloth. The product is washed while still on the funnel with cold glacial acetic acid until the washings are practically colorless. In order to effect rapid drying, the acetic acid is finally washed out of the filter cake by means of 100–200 ml. of ether. The yellow alloxan monohydrate weighs 120–125 g. (75–78%) after drying; m.p. 254° (dec.). It is pure enough for most purposes (Note 3).

2. Notes

1. This amount was found to give best yields.
2. It is very important that the temperature does not rise above 50°. If the addition of barbituric acid is carried out too rapidly, the temperature rise cannot be checked satisfactorily and the yield may drop considerably.
3. If entirely pure alloxan monohydrate is desired, this material is recrystallized according to the directions in an earlier volume of this series.²

3. Methods of Preparation

The methods for the preparation of alloxan have been reviewed earlier.^{2,3} The present method is essentially that of Wenner.⁴

¹ Hoffmann-La Roche, Inc., Nutley, New Jersey.

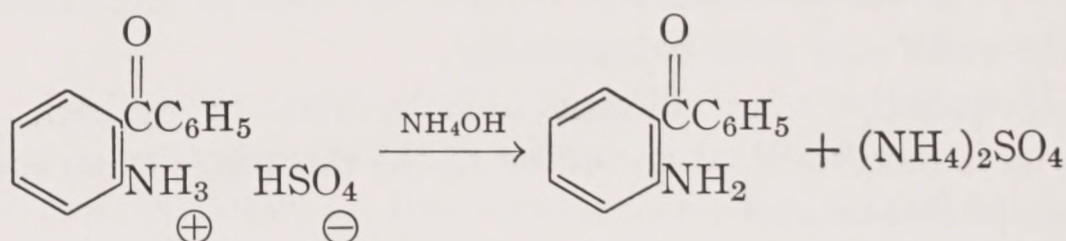
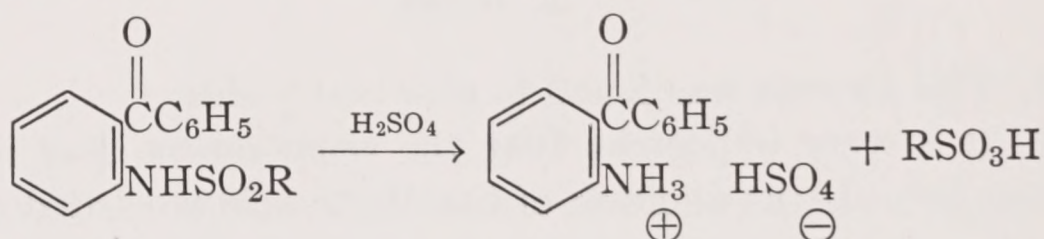
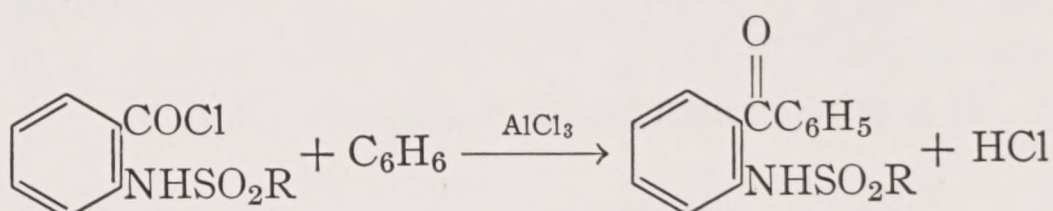
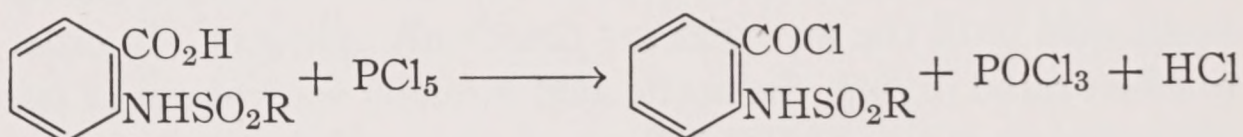
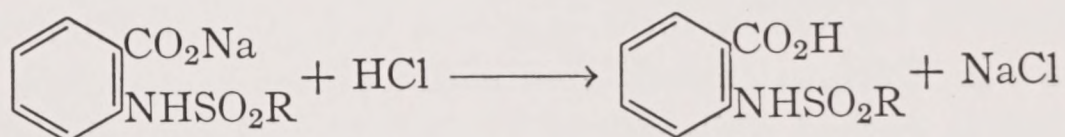
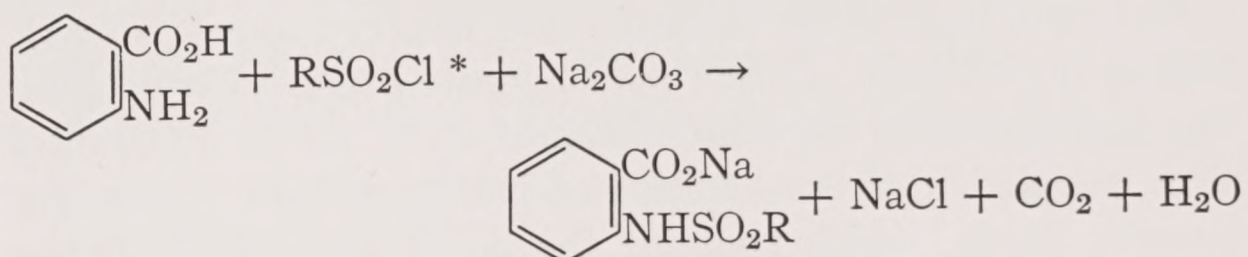
² *Org. Syntheses*, **21**, 5 (1941).

³ *Org. Syntheses*, **23**, 3 (1943).

⁴ Wenner, U. S. pat. 2,445,898 [*C. A.*, **43**, 2227 (1949)].

2-AMINOBENZOPHENONE

(Benzophenone, 2-amino-)



Submitted by H. J. SCHEIFELE, JR., and D. F. DETAR.¹
 Checked by R. T. ARNOLD and JOHN D. JONES.

1. Procedure

p-Toluenesulfonylanthranilic acid. In a 5-l. three-necked flask equipped with a stirrer and a thermometer extending to the bottom of the flask are placed 1.5 l. of water and 260 g. (2.4

* R = *p*-CH₃C₆H₄—.

moles) of technical grade dry sodium carbonate (Note 1). While the mixture is warmed, 137 g. (1.00 mole) of anthranilic acid is added in three portions, and the temperature is raised to 70° to effect complete solution. The solution is allowed to cool to about 60°, and 230 g. (1.21 moles) of technical *p*-toluenesulfonyl chloride is added in 5 portions over a period of about 20 minutes (Note 2). When all the *p*-toluenesulfonyl chloride has been added, the reaction mixture is maintained at 60–70° for an additional 20 minutes. The temperature is raised to about 85°, 10 g. of Norit is added cautiously, and the solution is filtered by suction through a previously heated Büchner funnel.

In a 4-l. beaker equipped with a stirrer which can be operated above the liquid level to break the foam are placed 250 ml. of 12 *N* hydrochloric acid and 250 ml. of water. The filtrate obtained above is cooled to about 50° and is added to the hydrochloric acid in small portions and at such a rate that the mixture does not foam over. If efficient stirring is used in the foam layer, this addition can be carried out in 5 minutes. The product is isolated by filtration through a Büchner funnel and is washed on the filter, first with a 250-ml. portion of dilute hydrochloric acid (prepared by diluting 50 ml. of 12 *N* hydrochloric acid to about 250 ml.) to remove anthranilic acid, and then with 500 ml. of water. The product is sucked as dry as possible and is then spread in a thin layer and allowed to air dry for about 15 hours. When easily pulverizable, the material is transferred to an oven and dried for 3 hours at 100–120°.

There is obtained 257–265 g. (88–91%) of *p*-toluenesulfonylanthranilic acid as a pale lavender powder with a neutral equivalent of 294–300, which indicates a purity of 97–99% (Note 3). This product is suitable for conversion to 2-aminobenzophenone, but it may be recrystallized by dissolving in hot 95% ethanol (10 ml. per g.) and then adding water (4 ml. per g.). The recovery in the first crop is about 75% of material melting at 229–230° and having a neutral equivalent of 295.

2-Aminobenzophenone. In a dry 3-l. three-necked flask equipped with a stirrer, a reflux condenser connected to a hydrogen chloride trap, and a thermometer extending to the bottom of the flask are

placed 146 g. (0.50 mole) of dry *p*-toluenesulfonylanthranilic acid, 1.5 l. of thiophene-free benzene, and 119 g. (0.57 mole) of phosphorus pentachloride. The mixture is stirred and heated at about 50° for 30 minutes. The murky solution (Note 4) is then cooled to 20–25°, and 290 g. (2.2 moles) of anhydrous aluminum chloride is added in 4 portions. When addition is complete, the dark mixture is heated with stirring at about 80–90° for 4 hours. The mixture is cooled to room temperature and poured onto a mixture of 500 g. of ice and 40 ml. of 12 *N* hydrochloric acid in a 5-l. round-bottomed flask. The benzene is best removed by vacuum distillation using a water aspirator (Note 5). The grainy brown crude product is separated by filtration on a Büchner funnel and washed thoroughly with dilute hydrochloric acid, with water, then with two 500-ml. portions of 5% sodium carbonate (to remove anthranilic acid and starting material), and finally with three 500-ml. portions of water (Note 6). The filter cake is sucked reasonably dry.

The crude, moist sulfonamide is dissolved in 1.6 l. of concentrated sulfuric acid by warming on the steam bath for 15 minutes. The sulfuric acid solution is divided into two equal parts, each of which is placed in a 4-l. beaker. The beakers are cooled in ice baths while 1.6 kg. of ice is added slowly and with stirring to the contents of each beaker. During the addition of the ice, phenyl *p*-tolyl sulfone separates. A total of 50 g. of Norit is added, and the solution is filtered (Notes 7 and 8).

The filtrates are best neutralized separately. Two 5-gal. crocks are half filled with crushed ice, and one-half of the total filtrate is poured into each. For neutralization, commercial 12 *N* ammonium hydroxide is added slowly with stirring; a total of 4.8 l. is required. The solid is collected on a Büchner funnel, washed with water, and air-dried.

The product is obtained in the form of bright yellow crystals, m.p. 103–105°. The yield is 68–71 g. (69–72% based on *p*-toluenesulfonylanthranilic acid). This material is dissolved in 1 l. of hot 95% ethanol, treated with 15 g. of Norit, and filtered. The hot solution is diluted with 700 ml. of hot water and cooled. After a second recrystallization, the yield of hexagonal yellow

plates is 47 g.; m.p. 105–106°. Another 6 g. of pure aminoketone can be recovered from the filtrate. The total yield of recrystallized 2-aminobenzophenone is 53 g. (54%) (Note 9).

2. Notes

1. If sodium hydroxide is used, the main product is the *p*-toluenesulfonic acid salt of anthranilic acid. This salt has properties quite similar to those of the desired *p*-toluenesulfonylanthranilic acid but is useless for the preparation of 2-aminobenzophenone.

2. It is advisable to have sodium hydroxide solution available in case carbon dioxide is evolved indicating that the amount of sodium carbonate used was insufficient.

There is a tendency for salts to precipitate from the mixture and for some foaming to occur if much less water is used.

3. The melting point of the *p*-toluenesulfonylanthranilic acid is not a good criterion of purity because the *p*-toluenesulfonic acid salt of anthranilic acid has about the same value. The neutral equivalents are widely different: 154 for the salt and 291 for *p*-toluenesulfonylanthranilic acid. The compound obtained in this preparation gives a negative test for anthranilic acid on diazotization and treatment with alkaline β -naphthol solution. The probable impurity is the sodium salt of *p*-toluenesulfonylanthranilic acid.

4. When recrystallized *p*-toluenesulfonylanthranilic acid is used, the solution is clear at this point. The crude acid gives rise to a dark solution containing a small amount of suspended solid. The yield of 2-aminobenzophenone is the same in either case.

5. Steam distillation may also be used but should not be prolonged. If the contents of the flask are kept below 80°, the crude product is obtained as a fine powder. If the temperature becomes too high, the material melts and anthranilic acid is not easily removed from the solid mass obtained on cooling.

6. It is convenient to keep the wash solutions at 75–80°, but the temperature should not exceed 85° or part of the organic material will melt and clog the filter. It is advisable to transfer

the solid to a 2-l. beaker to permit thorough washing. Most of the wash solution can be separated by decantation.

7. Phenyl *p*-tolyl sulfone may be isolated at this point by filtering the acid solution before using Norit. It can be purified by recrystallization from 95% ethanol; m.p. 125°.

8. The temperature of the solution should be 30–35°. If too cold some of the product will be retained on the filter, and if too hot the filter paper is attacked by the acidic solution. 2-Aminobenzophenone is a weak base and separates as the free base from sulfuric acid solutions below about 4 *N*.

9. 4'-Methyl-2-aminobenzophenone can be prepared similarly by substituting toluene for benzene. The yield of crude material, m.p. 85–88°, is 70%. On recrystallization from 95% ethanol, using 5 ml. per g., there is obtained, in two crops, a 70% recovery of 4'-methyl-2-aminobenzophenone, m.p. 92–93°. Because of the higher temperature required in the steam distillation (cf. Note 5), the sulfonamide is obtained in a form difficult to purify. As a result the crude aminoketone usually contains 1–2 g. of aluminum oxide.

3. Methods of Preparation

The above procedure is essentially that of Ullmann and Bleier.² 2-Aminobenzophenone has also been prepared by reduction of 2-nitrobenzophenone,³ by the Hofmann reaction of the amide of *o*-benzoylbenzoic acid with sodium hypobromite,⁴ by the action of an excess of benzoyl chloride on aniline at 220°,⁵ and by hydrolysis of the acetyl derivative which is obtained by the action of phenylmagnesium bromide on 2-methyl-3,1,4-benzoxaz-4-one (from anthranilic acid and acetic anhydride).⁶ Various methods for the preparation of 2-aminobenzophenones have been summarized critically by Simpson, Atkinson, Schofield, and Stephenson.⁷

¹ Cornell University, Ithaca, New York.

² Ullmann and Bleier, *Ber.*, **35**, 4273 (1902); cf. also Stoermer and Finche, *Ber.*, **42**, 3118 (1909).

³ Geigy and Koenigs, *Ber.*, **18**, 2400 (1885); Tatschaloff, *J. prakt. Chem.*, [2] **65**, 308 (1902); Gabriel and Stelzner, *Ber.*, **29**, 1300 (1896).

⁴ Graebe and Ullmann, *Ann.*, **291**, 8 (1896). (The submitters have found that the Curtius procedure gives better results than the method of Hofmann; cf. P. A. S.

Smith, in Adams, *Organic Reactions*, Vol. 3, p. 337, John Wiley & Sons, New York, 1946.)

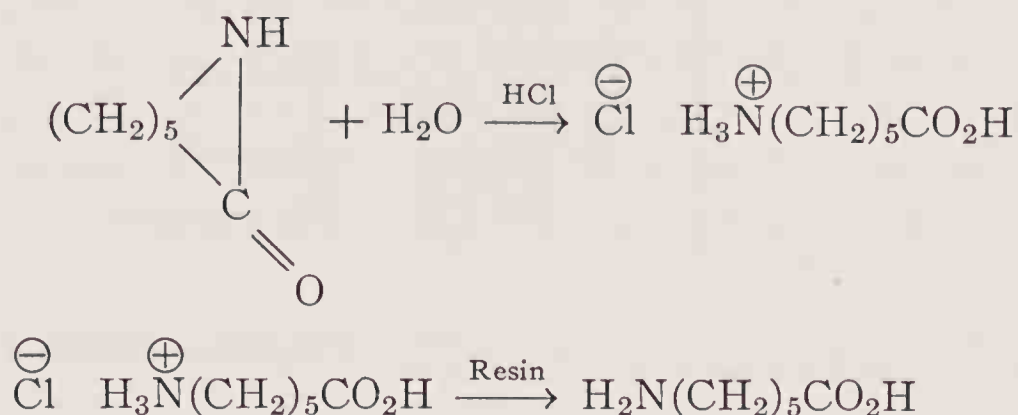
⁵ Chattaway, *J. Chem. Soc.*, **85**, 386 (1904).

⁶ Lothrop and Goodwin, *J. Am. Chem. Soc.*, **65**, 363 (1943).

⁷ Simpson, Atkinson, Schofield, and Stephenson, *J. Chem. Soc.*, **1945**, 646.

ε-AMINOCAPROIC ACID

(Caproic acid, ε-amino)



Submitted by CAL Y. MEYERS and LEONARD E. MILLER.¹

Checked by RICHARD T. ARNOLD and WILLIAM R. HASEK.

1. Procedure

Into a 500-ml. round-bottomed flask containing 50 g. (0.44 mole) of 2-ketohexamethylenimine (ε-caprolactam) is poured a solution containing 45 ml. of concentrated hydrochloric acid (sp. gr. 1.19) dissolved in 150 ml. of water. The mixture is boiled for 1 hour, and the resulting yellow solution is decolorized with Norit and evaporated to dryness under reduced pressure on a steam bath (Note 1).

The resulting ε-aminocaproic acid hydrochloride is converted into the amino acid by means of a column containing Amberlite IR-4B resin (Note 2):

1. Construct the column as shown in Fig. 1.

2. *Exhaustion.* Pass a 1% aqueous hydrochloric acid solution through the column (downflow) until the pH of the solution leaving the column decreases from 5.5–6.5 to about 2.

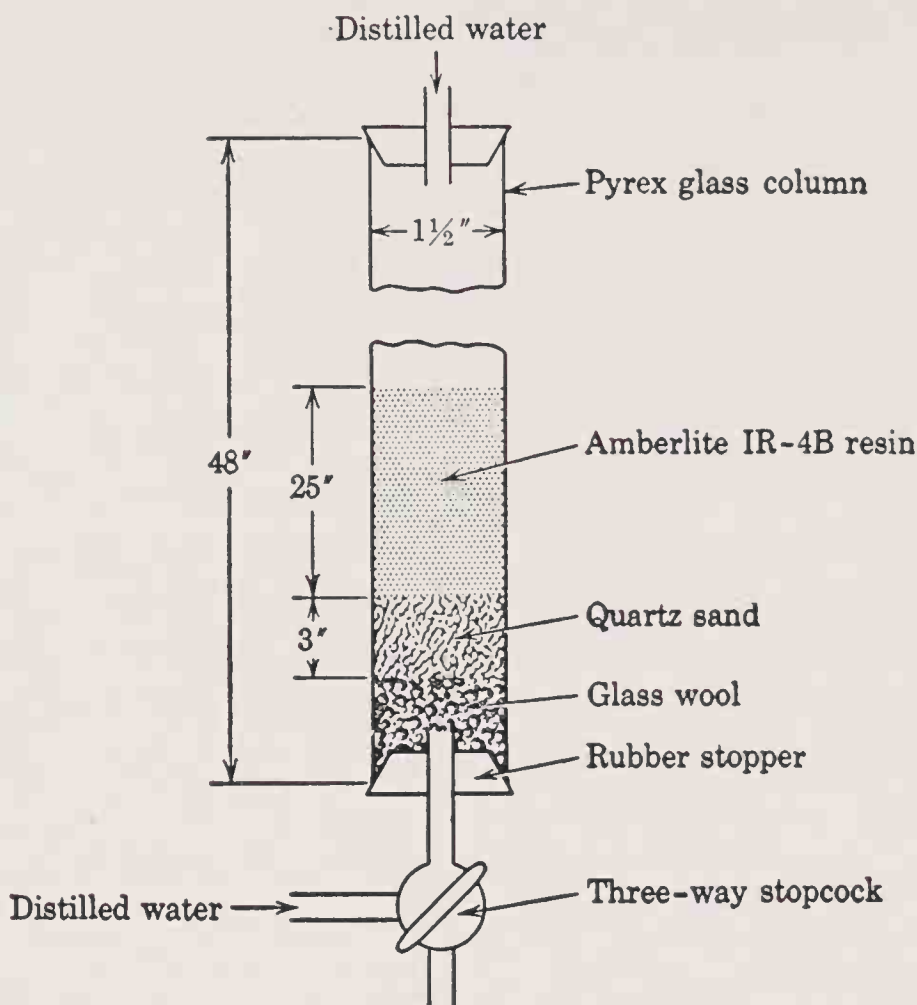


FIG. 1.

3. *Regeneration.* Now pass a 1% aqueous sodium hydroxide solution through the column (downflow) until the solution leaving the column is strongly alkaline.

4. *Classification.* Wash the resin (upflow) with 10 l. of distilled water.

5. Wash the resin with distilled water (downflow) (Note 3) until the salts are all washed out and the *pH* of the washings is 5.6–6.5. The column is now ready for use (Note 4).

The solid ϵ -aminocaproic acid hydrochloride is dissolved in 1 l. of distilled water. This solution is passed through the column (downflow) and followed by at least 2 l. of distilled water (Note 5).

The collected solution (pink) is concentrated by distillation, under reduced pressure, to a volume of about 100 ml. (Note 6), and the resulting orange-colored solution is decolorized with Norit. After the addition of 300 ml. of absolute ethanol and 500 ml. of ether, followed by vigorous shaking, a white solid forms within a few minutes. The ϵ -aminocaproic acid is collected

on a Büchner funnel and dried in a vacuum desiccator until no more ether-alcohol odor is detected. A yield of 52 g. (90%) is obtained; m.p. 202–203°.

2. Notes

1. This hydrolysis is similar to that utilized previously.²
2. Obtained from the Resinous Products Division, Rohm and Haas Company, Philadelphia, Pennsylvania. The checkers found that this resin sometimes liberates carbon dioxide when treated with 1% hydrochloric acid. In such cases the total resin sample may be pretreated in a beaker with 1% hydrochloric acid until no more gas is evolved, and then a 30-in. (rather than 25-in.) column containing 1% hydrochloric acid is packed with resin. Further treatment of the resin is continued as described by the submitters.
3. Intermittent silver nitrate tests will indicate whether the solution is free of salts.
4. The liquid level of the column should always be above the resin when the column is not in use.
5. To assure the user that the resin is functioning, the eluant should be tested frequently for *pH* and the presence of salts. If the test for chloride ion becomes positive, or if the *pH* falls below 5.6, regeneration procedures are necessary; generally the column is good for two runs.
6. Excessive heating and excessive evaporation may result in peptide formation.

3. Methods of Preparation

ϵ -Aminocaproic acid has been prepared by the hydrolysis of ϵ -benzoylaminocapronitrile,³ by the hydrolysis of diethyl ω -phthalimidobutylmalonate,⁴ from cyclohexanone oxime by rearrangement and hydrolysis,⁵ and by hydrochloric acid hydrolysis of ϵ -caprolactam and removal of the acid by the use of litharge, silver oxide, etc.²

¹ University of Illinois, Urbana, Illinois.

² *Org. Syntheses* Coll. Vol. 2, 28 (1943).

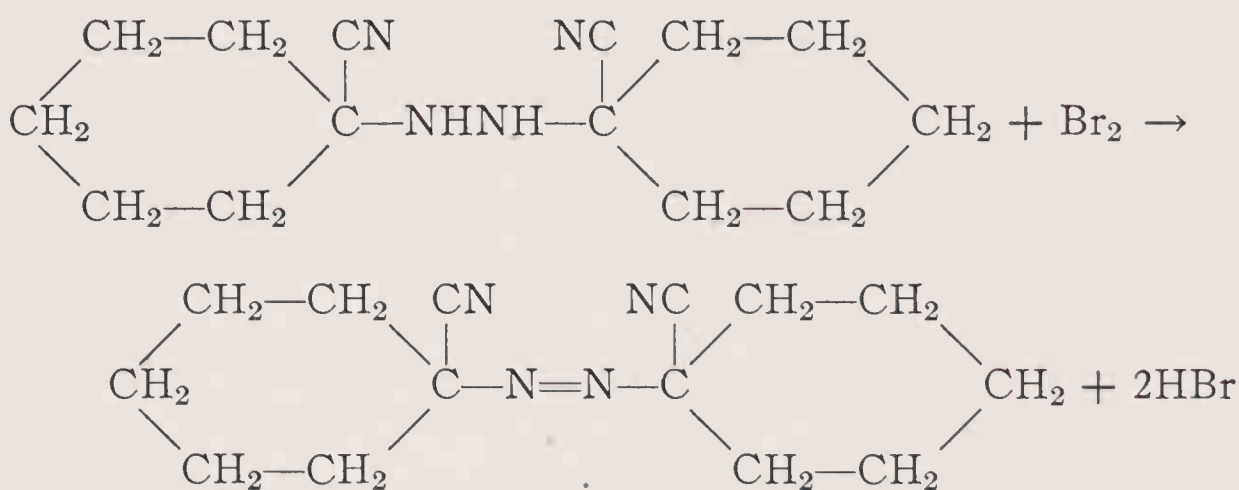
³ von Braun and Steindorff, *Ber.*, **38**, 177 (1905); von Braun, *Ber.*, **40**, 1839 (1907); Ruzicka and Hugoson, *Helv. Chim. Acta*, **4**, 479 (1921); Marvel, Mac-Corquodale, Kendall, and Lazier, *J. Am. Chem. Soc.*, **46**, 2838 (1924).

⁴ Gabriel and Maass, *Ber.*, **32**, 1266 (1899).

⁵ Wallach, *Ann.*, **312**, 188 (1900); Eck and Marvel, *J. Biol. Chem.*, **106**, 387 (1934).

1,1'-AZO-bis-1-CYCLOHEXANENITRILE

(Cyclohexanecarbonitrile, 1,1'-azodi-)



Submitted by C. G. OVERBERGER, PAO-TUNG HUANG, and M. B. BERENBAUM.¹

Checked by N. J. LEONARD and E. H. MOTTUS.

1. Procedure

In a 600-ml. beaker equipped with a stirrer, thermometer, and dropping funnel are placed 24.6 g. (0.1 mole) of finely powdered 1,2-di-1-(1-cyano)-cyclohexylhydrazine (p. 50) and 130 ml. of 90% ethanol. To this mixture is added slowly, with cooling, 45 ml. of concentrated hydrochloric acid. The beaker is placed in an ice bath, and, after the suspension has been cooled to 10°, bromine is added at such a rate that the temperature does not rise above 15°. About 16–17 g. (about 0.1 mole) of bromine is required to reach the end point characterized by a permanent orange-yellow color. The reaction mixture is poured into 80 ml. of ice water. After 15 minutes the suspension is filtered with the aid of a Büchner funnel, washed with 250 ml. of water, and pressed dry. The solid is transferred to a 500-ml. Erlenmeyer flask, 120 ml. of boiling 95% ethanol is added, and the crude

product is dissolved as rapidly as possible while being heated on a steam bath (Note 1). The solution is filtered through a fluted filter in a heated funnel, and the filtrate is placed in a refrigerator overnight. The solid is collected on a Büchner funnel and dried in a vacuum desiccator over calcium chloride. The yield of product is 20.5–22.0 g. (84–90%); m.p. 113.5–115.5° (Notes 2 and 3).

2. Notes

1. Prolonged heating of the solution will cause excessive decomposition of the azo compound.

2. This compound is stable indefinitely if stored at room temperature. Prolonged heating at temperatures of 80° or higher, however, will result in rapid decomposition involving possible hazards.²

3. 2,2'-Azo-*bis*-isobutyronitrile can be prepared in a similar manner. The product after recrystallization from 95% ethanol is obtained in a yield of 85–90%; m.p. 102–103°. This compound must be regarded as an explosive.²

3. Methods of Preparation

1,1'-Azo-*bis*-1-cyclohexanenitrile has been prepared in a similar manner by Hartman.³ The method has been substantiated by Overberger, O'Shaughnessy, and Shalit⁴ and is a modification of that used originally by Thiele and Heuser⁵ for the synthesis of 2,2'-azo-*bis*-isobutyronitrile.

¹ Polytechnic Institute of Brooklyn, Brooklyn, New York.

² Carlisle, *Chem. Eng. News*, **27**, 150 (1949); **28**, 803 (1950).

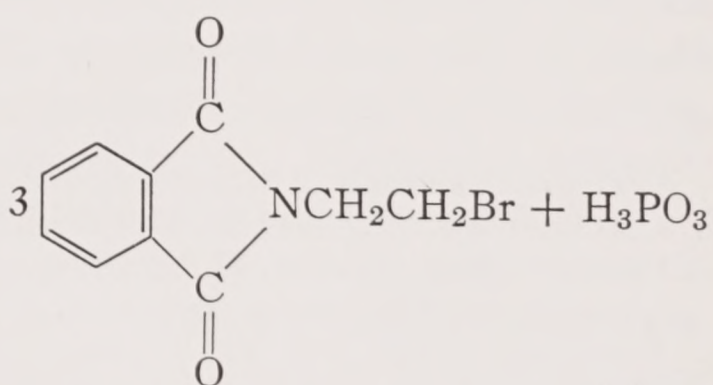
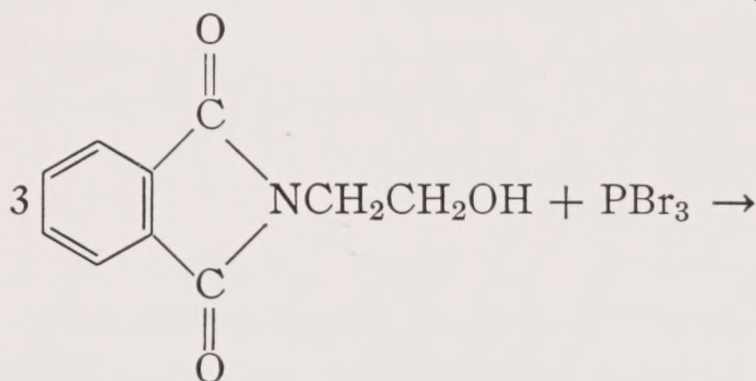
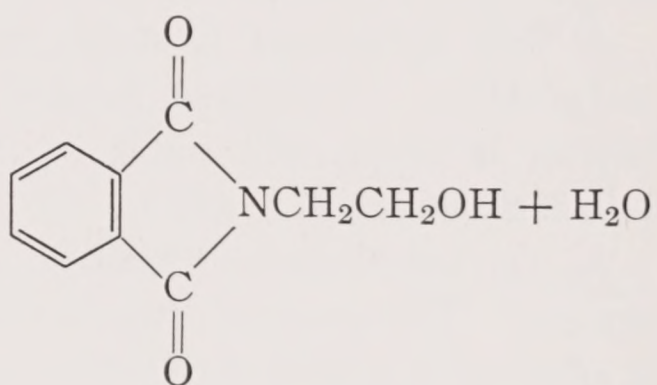
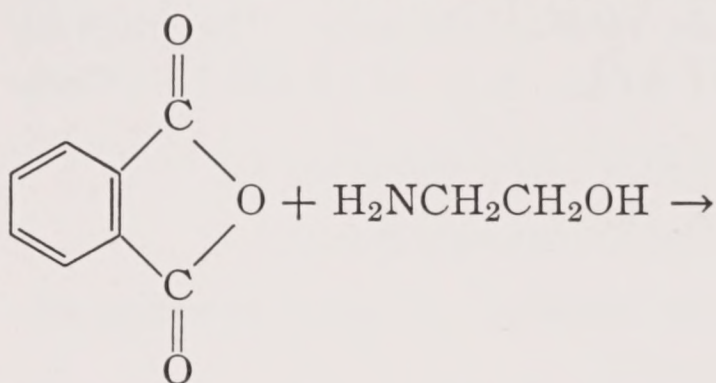
³ Hartman, *Rec. trav. chim.*, **46**, 150 (1927).

⁴ Overberger, O'Shaughnessy, and Shalit, *J. Am. Chem. Soc.*, **71**, 2661 (1949).

⁵ Thiele and Heuser, *Ann.*, **290**, 1 (1896).

β-BROMOETHYLPHTHALIMIDE

(Phthalimide, N-2-bromoethyl-)

Submitted by T. O. SOINE and M. R. BUCHDAHL.¹

Checked by CLIFF S. HAMILTON and JOHN D. SCULLEY.

1. Procedure

Caution! This preparation should be carried out in a hood.

In a 1-l. round-bottomed flask are placed 74 g. (0.5 mole) of phthalic anhydride and 30 ml. (0.5 mole) of freshly distilled monoethanolamine. The mixture is heated on a steam bath for 30 minutes; the initial reaction is vigorous (Note 1). The reaction mixture is cooled to room temperature, and a reflux condenser is attached to the flask. To the cooled reaction mixture is added slowly, with shaking, 32 ml. (91.3 g., 0.337 mole) of freshly distilled phosphorus tribromide. The reaction flask is then placed on a steam bath and heated under reflux with occasional shaking for 1.25 hours (Note 2). The hot liquid reaction mixture is poured with stirring onto 750 g. of crushed ice. When the ice has melted completely, the crude β -bromoethylphthalimide is collected on a Büchner funnel, washed with cold water, and allowed to dry for a few minutes. The crude product (Note 3) is dissolved in 1.2 l. of aqueous ethanol (50% by volume) with the aid of heat. If necessary a small amount of 95% ethanol is added to effect complete solution. The hot solution is filtered and cooled in a refrigerator. A white crystalline product weighing 94–99 g. is obtained. Concentration of the mother liquor to 400 ml. yields an additional 1–3 g. of product. The total yield of product is 95–102 g. (75–80%); m.p. 80–82°.

2. Notes

1. It is not necessary to isolate the intermediate β -hydroxyethylphthalimide before going on to the next step. However, recrystallization of the product from 250 ml. of boiling water yields an initial crop of white crystals; m.p. 128°. The mother liquors will deposit further material until a yield of 95% may be obtained.

2. The final reaction mixture should contain no undissolved material.

3. This product weighs approximately 110 g. when dry.

3. Methods of Preparation

β -Bromoethylphthalimide has been prepared by the method of Gabriel² as recorded by Salzberg and Supniewski.³ The procedure outlined above is a modification of the method given by Soine.⁴

¹ University of Minnesota, Minneapolis, Minnesota.

² Gabriel. *Ber.*, **20**, 2224 (1887); **21**, 566 (1888); **22**, 1137 (1889).

³ *Org. Syntheses* Coll. Vol. **1**, 119 (1941).

⁴ Soine, *J. Am. Pharm. Assoc.*, **33**, 141 (1944).

tert-BUTYL HYPOCHLORITE



Submitted by H. M. TEETER and E. W. BELL.¹

Checked by CHARLES C. PRICE and T. C. SCHWANN.

1. Procedure

Caution! This preparation should be carried out in a good hood. The product should be protected from strong light, overheating, or exposure to rubber to avoid vigorous decomposition.

A solution of 80 g. (2 moles) (Note 1) of sodium hydroxide in about 500 ml. of water is prepared in a 2-l. three-necked round-bottomed flask equipped (Note 2) with a gas inlet tube reaching nearly to the bottom of the flask, a gas outlet tube, and a mechanical stirrer. The flask is placed in a water bath at 15–20° (Note 3), and, after the contents have cooled to this temperature, 74 g. (96 ml., 1 mole) of *tert*-butyl alcohol (Note 4) is added together with enough water (about 500 ml.) to form a homogeneous solution. With constant stirring, chlorine is passed into the mixture for 30 minutes at a rate of approximately 1 l. per minute (Note 5) and then for an additional 30 minutes at a rate of 0.5–0.6 l. per minute.

The upper oily layer is then separated with the aid of a separatory funnel (Note 6). It is washed with 50-ml. portions of 10%

sodium carbonate solution until the washings are no longer acidic to Congo red. It is finally washed 4 times with an equal volume of water and dried over calcium chloride. The yield is 78–107 g. (72–99%) (Note 7); d_{20}^{20} 0.910; n_D^{20} 1.403. The product is best stored under an inert atmosphere (Note 8) in sealed bottles kept in the dark in a refrigerator (Note 9).

2. Notes

1. The submitters have successfully carried out this preparation in quantities up to 7 moles (519 g.) of *tert*-butyl alcohol using 2.25 hours for the addition of chlorine at each rate.

2. *tert*-Butyl hypochlorite reacts violently with rubber. The apparatus should therefore be assembled by means of ground-glass joints. Synthetic plastic tubing (Tygon) may be used instead of rubber tubing.

3. For 7-mole runs, a satisfactory bath consists of a 10-gal. earthenware jar fitted with a water inlet and an overflow device. The desired temperature is obtained by adjusting the rate of flow of tap water through the jar. The reaction can also be carried out successfully using an ice-water bath.

4. The *tert*-butyl alcohol was a commercial product obtained from the Shell Chemical Corporation, New York, New York.

5. Rates of flow are conveniently measured with the usual U-tube and capillary using one of the liquid Arochlors as the indicating fluid. The checkers did not use a flow meter but passed in chlorine rapidly at first and then slowly for 30 minutes after the initial rapid absorption.

6. In 7-mole runs carried out by the submitter, the bulk of the aqueous layer was removed conveniently by siphoning through the gas inlet tube.

7. This product, which is sufficiently pure for most purposes, contains about 2% free chlorine. It may be purified by distillation in an all-glass apparatus heated by a steam bath. The yield of pure product is 75–104 g. (69–96%); b.p. 77–78°/760 mm. Active chlorine assay indicates 97–98% purity for the crude product, 98–100% purity for the distilled material.

8. The inert atmosphere helps to minimize any tendency of vapors to ignite during sealing of the bottle. Filled bottles should be cooled in solid carbon dioxide before sealing.

9. When exposed to light, *tert*-butyl hypochlorite decomposes with formation of acetone and methyl chloride. When induced by radiation from an ultraviolet lamp, this decomposition proceeds rapidly enough to raise the temperature of the hypochlorite to the boiling point. The decomposition does not continue after irradiation is stopped. Customary room illumination does not induce the decomposition to a noticeable extent during ordinary handling of this material. However, a sealed glass bottle of hypochlorite should not be allowed to stand in light for a prolonged time as pressure sufficient to burst the bottle may be built up gradually.

3. Methods of Preparation

tert-Butyl hypochlorite has been prepared by the action of chlorine upon alkaline solutions of *tert*-butyl alcohol.^{2, 3, 4, 5} Solutions of *tert*-butyl hypochlorite have been prepared by shaking a solution of the alcohol in carbon tetrachloride with aqueous hypochlorous acid.⁶ The procedure described is that used by Teeter et al.⁴

¹ Northern Regional Research Laboratory, U. S. Department of Agriculture, Peoria, Illinois.

² Chattaway and Backeberg, *J. Chem. Soc.*, **1923**, 2999.

³ Irwin and Hennion, *J. Am. Chem. Soc.*, **63**, 858 (1941).

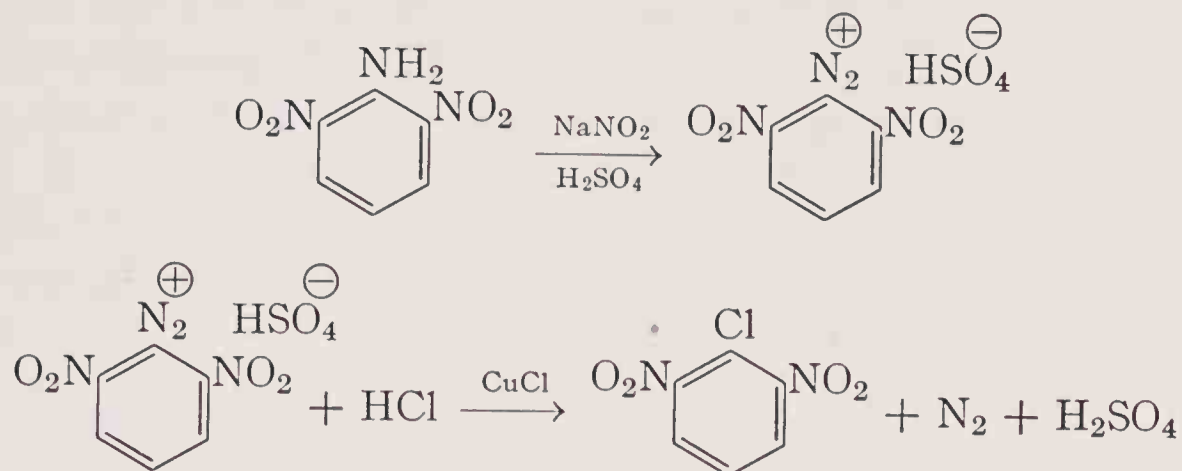
⁴ Teeter, Bachmann, Bell, and Cowan, *Ind. Eng. Chem.*, **41**, 848 (1949).

⁵ Deanesly, U. S. pat. 1,938,175 [*C. A.*, **28**, 1053 (1934)].

⁶ Taylor, MacMullin, and Gammal, *J. Am. Chem. Soc.*, **47**, 395 (1925).

1-CHLORO-2,6-DINITROBENZENE

(Benzene, 2-chloro-1,3-dinitro-)

Submitted by F. D. GUNSTONE and S. HORWOOD TUCKER.¹

Checked by ARTHUR C. COPE, DAVID J. MARSHALL, and RONALD M. PIKE.

1. Procedure

Concentrated sulfuric acid (160 ml.) is placed in a 1-l. three-necked flask fitted with a glass stirrer and a thermometer, and 15.2 g. (0.22 mole) of solid sodium nitrite is added over a period of 10–15 minutes with stirring. After the addition is completed, the temperature is raised to 70° and the mixture is stirred until all the sodium nitrite dissolves. The solution is cooled to 25–30° with an ice bath, and a solution of 36.6 g. (0.2 mole) of 2,6-dinitroaniline² in 400 ml. of hot glacial acetic acid is added slowly, with stirring, at such a rate that the temperature remains below 40° (Note 1). After the addition is completed, the solution is stirred at 40° for 0.5 hour. A solution of 44 g. (0.44 mole) of cuprous chloride in 400 ml. of concentrated hydrochloric acid is prepared in a 2-l. beaker and cooled in an ice bath, and the solution of the diazonium salt is added in portions over a period of about 5 minutes, with manual stirring, at a rate which keeps the effervescence from becoming too vigorous. The mixture becomes hot during the addition, and it is stirred intermittently while being cooled in an ice bath until the effervescence slackens. It is then heated on a steam bath with occasional stirring until

the temperature reaches 80°. After about 20 minutes at that temperature the effervescence ceases, and then an equal volume of water is added and the mixture is cooled in an ice bath. After several hours the yellow, crystalline 1-chloro-2,6-dinitrobenzene is collected on a suction filter, washed with water, and dried (Note 2). The product, which is sufficiently pure for most purposes without recrystallization, is obtained in a yield of 28.7–30 g. (71–74%); m.p. 86–88°. The product can be recrystallized from 90% (by volume) acetic acid (2 ml. per g.) or by dissolving it in hot benzene (1.5 ml. per g.) and adding petroleum ether (3 ml. per g.); m.p. 86–87°.

2. Notes

1. The temperature of diazotization is critical. Lower yields are obtained if the temperature rises above 40°.

2. 1-Chloro-2,6-dinitrobenzene is a skin irritant, and contact with it should be avoided.

3. Methods of Preparation

1-Chloro-2,6-dinitrobenzene has been prepared from 2,6-dinitroaniline by the Sandmeyer reaction,^{3, 4} and from the mixture of isomers (in which 1-chloro-2,4-dinitrobenzene is present in largest amount) obtained by nitrating *o*-nitrochlorobenzene.^{4, 5}

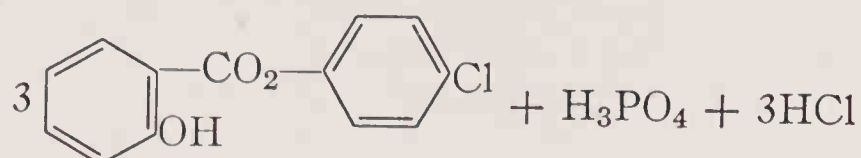
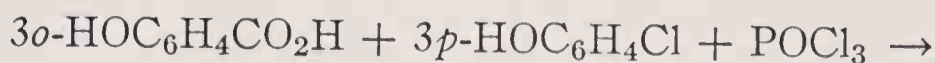
¹ The University, Glasgow, Scotland.

² *Org. Syntheses*, **31**, 45 (1951).

³ Welsh, *J. Am. Chem. Soc.*, **63**, 3276 (1941).

⁴ Hodgson and Dodgson, *J. Chem. Soc.*, **1948**, 1006.

⁵ Borsche and Rantscheff, *Ann.*, **379**, 152 (1911).

p-CHLOROPHENYL SALICYLATE(Salicylic acid, *p*-chlorophenyl ester)Submitted by NORMAN G. GAYLORD and P. M. KAMATH.¹

Checked by R. T. ARNOLD and J. JOHN BREZINSKI.

1. Procedure

To a mixture of 138.1 g. (1 mole) of salicylic acid and 128.6 g. (1 mole) of *p*-chlorophenol in a 2-l. round-bottomed flask fitted with a thermometer reaching to the bottom of the flask and a reflux condenser with a drying tube (Note 1) is added 58.3 g. (0.38 mole) of phosphorus oxychloride. The mixture is heated with occasional swirling, and the temperature is maintained at 75–80°. At the end of 4 hours the reactants have been reduced to a molten mass, and this is poured slowly, with vigorous stirring, into a solution of 120 g. of sodium carbonate in 800 ml. of water. The precipitated ester is collected on a filter and washed with four 200-ml. portions of water. The yield of crude, air-dried, *p*-chlorophenyl salicylate is 174–189 g. (70–76%); m.p. 65–66°. Recrystallization from absolute ethanol yields 136–154 g. (55–62%) of pure product; m.p. 69.5–70.5°. A second crop may be obtained by concentration of the filtrate from the first crop or by the addition of water (Note 2).

2. Notes

1. It is advisable to attach the drying tube to a water trap² in order to prevent the escape of hydrogen chloride into the atmosphere.

2. The above method has been used in the preparation of other substituted phenyl salicylates to give the following yields of recrystallized products with the indicated melting points.

	YIELD (%)	M.P.
<i>o</i> -Chlorophenyl ester	67	52.0– 52.4°
<i>p</i> -Nitrophenyl ester	53	151.5–151.9°
<i>p-tert</i> -Butylphenyl ester	42	63.0– 63.4°
<i>p</i> -Phenylphenyl ester	66	109.2–109.6°
<i>o</i> -Phenylphenyl ester	70	89.2– 89.5°

These esters, with the exception of the *p*-nitrophenyl derivative, can be recrystallized from absolute ethanol. The nitro compound is recrystallized from dioxane.

3. Methods of Preparation

Substituted phenyl salicylates can be prepared by heating salicylic acid and the appropriate phenol in the presence of phosphorus oxychloride,^{3, 4, 5} phosphorus trichloride,^{4, 5} phosphorus pentachloride,^{4, 6} phosgene,⁴ or thionyl chloride,⁴ or by heating the phenol and salol.⁷

¹ Polytechnic Institute of Brooklyn, Brooklyn, New York.

² *Org. Syntheses* Coll. Vol. **1**, 97 (1941).

³ Siefert, *J. prakt. Chem.*, [2] **31**, 472 (1885); Nencki and Heyden, Ger. pat. 38,973 [*Ber.*, **20R**, 351 (1887)], and Ger. pat. 43,713 [*Ber.*, **21R**, 554 (1888)]; Walther and Zipper, *J. prakt. Chem.*, [2] **91**, 399 (1915); Krauz and Remenec, *Collection Czechoslov. Chem. Commun.*, **1**, 610 (1929) [*C. A.*, **24**, 1365 (1930)]; Kolloff and Page, *J. Am. Chem. Soc.*, **60**, 948 (1938).

⁴ Nencki and Heyden, Ger. pat. 70,519 [*Ber.*, **26R**, 967 (1893)].

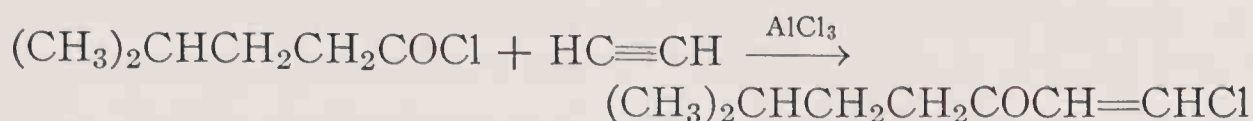
⁵ Harris and Christiansen, *J. Am. Pharm. Assoc.*, **24**, 553 (1935); U. S. pat. 2,141,172 [*C. A.*, **33**, 2655 (1939)].

⁶ Tozer and Smiles, *J. Chem. Soc.*, **1938**, 1897.

⁷ Cohn, *J. prakt. Chem.*, [2] **61**, 550 (1900).

β -CHLOROVINYL ISOAMYL KETONE

(1-Hepten-3-one, 1-chloro-6-methyl-)

Submitted by CHARLES C. PRICE and JOSEPH A. PAPPALARDO.¹

Checked by R. S. SCHREIBER, WM. BRADLEY REID, JR., and R. W. JACKSON.

1. Procedure

Caution! This preparation should be carried out in a good hood.

A 1-l. three-necked flask fitted with a mercury-sealed stirrer, a gas inlet tube, and a gas outlet tube protected by a calcium chloride drying tower (Note 1) is surrounded by an ice-water bath. The system is flushed slowly with acetylene for 3 minutes (Note 2). Carbon tetrachloride (260 g.) (Note 3) is poured into the flask, and acetylene is bubbled through at a saturation rate for 3 minutes. Aluminum chloride (98 g., 0.74 mole) (Note 4) is added, and acetylene is bubbled continuously through the mixture with stirring for 5 minutes.

The gas inlet tube is replaced by a dropping funnel protected by a calcium chloride drying tube. Isocaproyl chloride (84.7 g., 0.63 mole) (Note 5) is added to the reaction mixture with stirring over a period of 20 minutes. The dropping funnel is replaced by the gas inlet tube (inlet tube wiped with a dry towel), and, with stirring, acetylene is bubbled just below the surface of the mixture at a rate noticeably above the saturation rate. After 15 minutes to 1 hour the rate of absorption of acetylene suddenly becomes very rapid, and the acetylene is passed through as rapidly as it is absorbed (Note 6). The introduction of acetylene is continued for 30 minutes after the rapid absorption (which lasts 1–2 hours) has subsided.

The reaction mixture is poured with stirring onto a mixture of 700 g. of crushed ice and 300 ml. of a saturated solution of sodium chloride. The organic layer is separated, and the aqueous layer

is extracted with three 100-ml. portions of ether. To the combined organic layers is added 2 g. of hydroquinone, and the mixture is dried over calcium chloride (Note 7).

The liquid is decanted from the solid, and the solid is washed with 50 ml. of carbon tetrachloride. The carbon tetrachloride layers are combined and 2 g. of hydroquinone is added. The solution is then distilled from a Claisen flask at such a pressure as to maintain a distillation temperature of about 30°. When most of the solvent has been removed it is discarded, and the residue is distilled as rapidly as possible until the temperature reaches about 90° at 5 mm. Redistillation from a Claisen flask with a short Vigreux side arm gives a colorless liquid; yield 55–65 g. (54–64%) (Note 8); b.p. 96–98°/20 mm.; n_D^{25} 1.4619 (Note 9).

2. Notes

1. A rubber tube with an eye-dropper is attached to the tower. The tip of the eye-dropper is immersed in mineral oil to indicate the absorption of acetylene.

2. The reaction is carried out in a well-ventilated hood to remove excess acetylene. All subsequent operations are also carried out in the hood because the product of the reaction has an objectionable odor. The acetylene used is passed through a train consisting of an empty 300-ml. bottle, a 300-ml. bottle containing 150 ml. of concentrated sulfuric acid (through which acetylene passes by means of a gas dispersion tube), a pressure-release valve, and another empty 300-ml. bottle.

3. Carbon tetrachloride (C.P. grade) decanted from calcium chloride was used.

4. Baker and Adamson Company powdered aluminum chloride was used.

5. Eastman Kodak Company white label isocaproyl chloride was redistilled and the middle 80% portion was used.

6. To keep the temperature in the immediate vicinity of the flask from rising, the ice bath should be stirred occasionally.

7. The combined organic layers should be allowed to stand in a separatory funnel about 30 minutes before drying because some additional water separates on standing.

8. The checkers consistently obtained yields of 75–76%.

9. This preparation works equally well for the isobutyl and isohexyl homologs. For β -chlorovinyl methyl ketone, which is both a lachrymator and a vesicant, the initial rapid rate of absorption of acetylene begins only after 3–9 hours.

3. Methods of Preparation

Carpmael,² Yakubovich and Merkulova,³ and Price and Pappalardo⁴ have used this general reaction to make β -chlorovinyl ketones from a variety of acid chlorides, employing various solvents and acidic catalysts. Bayer and Nelles⁵ made β -chlorovinyl ketones by the reaction of an acid chloride and vinyl chloride.

¹ University of Notre Dame, Notre Dame, Indiana.

² Carpmael, Brit. pat. 461,080 [C. A., **31**, 4676 (1937)].

³ Yakubovich and Merkulova, *J. Gen. Chem. U.S.S.R.*, **16**, 55 (1946) [C. A., **41**, 91 (1947)].

⁴ Price and Pappalardo, *J. Am. Chem. Soc.*, **72**, 2613 (1950).

⁵ Bayer and Nelles, U. S. pat. 2,137,664 [C. A., **33**, 1758 (1939)].

CYANOGEN IODIDE



Submitted by B. BAK and A. HILLEBERT.¹

Checked by R. T. ARNOLD and H. E. FRITZ.

1. Procedure

Caution! Cyanogen iodide is relatively volatile and highly toxic. Therefore, these operations should be conducted in a good hood.

A three-necked 500-ml. flask is surrounded by an ice-water bath and provided with a stirrer and thermometer. Twenty-seven grams (0.55 mole) of sodium cyanide is dissolved in 100 ml. of water, added to the reaction flask, and cooled to 0°. To this, in 3- to 4-g. portions, is added with good stirring a total of 127 g. (0.50 mole) of iodine over a period of 30–40 minutes. A

given portion of iodine is not added until the preceding one has reacted almost completely. Ten minutes after the addition of iodine is completed, 120 ml. of peroxide-free ether is added and the mixture is stirred for a few minutes until the precipitated cyanogen iodide has dissolved in the ethereal layer. The entire contents are then transferred to a previously cooled separatory funnel, and the aqueous layer is separated. This aqueous solution is again extracted successively with 100-ml. and 80-ml. portions of cold, peroxide-free ether. The combined ethereal extracts are poured into a 500-ml. round-bottomed flask, and the ether is evaporated under reduced pressure at room temperature. To the slightly brown crude product, which weighs about 90 g., is added 120 ml. of water. A slightly diminished pressure ($\frac{1}{2}$ atm.) is maintained while the contents in the closed flask are heated at 50° for 15 minutes with occasional vigorous shaking (Note 1). The mixture is then cooled to 0° , and the crystalline cyanogen iodide is separated from the light yellow mother liquor by suction on a sintered-glass funnel or filter plate (Note 2). The crude product is washed with six 25-ml. portions of ice water, removed from the sintered-glass funnel, and air-dried (in a good hood) for 1 hour at room temperature. Colorless cyanogen iodide weighing about 59 g. (77%) is obtained; m.p. $141-144^{\circ}$ (Note 3).

Cyanogen iodide of highest purity may be produced in the following way. The above crude product is dissolved in 150 ml. of boiling chloroform, and the solution is filtered through a plug of glass-wool on a hot-water funnel into a 250-ml. Erlenmeyer flask. This solution, after being cooled at room temperature for 15 minutes, is placed in an ice-salt bath and cooled to -10° (Note 4). By means of suction filtration, the crystalline product is collected on a sintered-glass funnel, washed with three 15-ml. portions of cold chloroform (0°), and freed from the last traces of solvent by being placed on a watch glass and exposed to the atmosphere (in a good hood) at room temperature for 1 hour. Practically colorless needle-shaped crystals weighing 45 g. (59%) are obtained; m.p. $146-147^{\circ}$ (Notes 3 and 5).

Removal of 100 ml. of chloroform from the above filtrate by means of evaporation under reduced pressure at room tempera-

ture and subsequent cooling permits isolation of an additional 2 g. of cyanogen iodide; m.p. 146–147°. The total yield thus becomes 47 g. (63% based on iodine).

2. Notes

1. In this way sodium iodide, soluble in the solution of cyanogen iodide in ether [complex formation of $\text{NaI}_2(\text{CN})$], is removed. This complex is avoided in the procedure by Ketelaar and Kruyer² in which chlorine is used. The method adopted here is faster and simpler and gives almost the same yield of purified cyanogen iodide.

2. Contact with filter paper must be avoided.

3. Determinations of the melting point of cyanogen iodide must be made using a sealed capillary which is kept totally immersed in the heating bath.

4. When the chloroform solution is cooled, a small aqueous layer is observed which finally separates as ice. The ice is filtered with cyanogen iodide but melts on the filter plate and is removed with the chloroform used as washing liquid.

5. Owing to the volatility of cyanogen iodide, the yield is slightly dependent on the speed of operation. By the above method sublimation as a means of purification is avoided. If, however, sublimation is desirable, it can be accomplished with appreciable speed only under reduced pressure and at temperatures at which cyanogen iodide is slowly decomposed into iodine and cyanogen. The vacuum must be constantly renewed during the operation.

3. Methods of Preparation

Cyanogen iodide has been prepared from mercuric cyanide and iodine,³ potassium cyanide and iodine,⁴ and sodium cyanide and iodine.⁵

¹ Universitetets Kemiske Laboratorium, Copenhagen K, Denmark.

² Ketelaar and Kruyer, *Rec. trav. chim.*, **62**, 550 (1943).

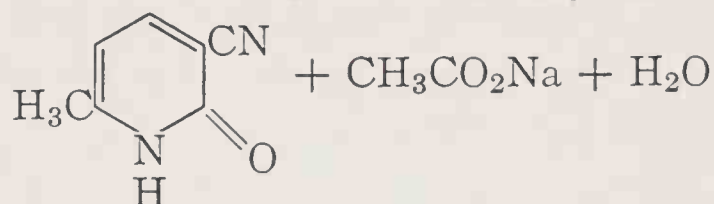
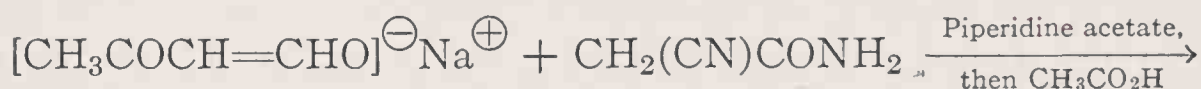
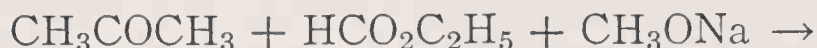
³ Seubert and Pollard, *Ber.*, **23**, 1062 (1890).

⁴ Grignard and Crouzier, *Bull. soc. chim. France*, [4] **29**, 214 (1921).

⁵ Moller, *Kgl. Danske Videnskab. Selskab, Math.-fys. Medd.*, **14**, 3 (1936).

3-CYANO-6-METHYL-2(1)-PYRIDONE

(Nicotinonitrile, 1,2-dihydro-6-methyl-2-oxo-)

Submitted by RAYMOND P. MARIELLA.¹

Checked by ARTHUR C. COPE, JAMES E. KRUEGER, and DAVID J. MARSHALL.

1. Procedure

In a 2-l. three-necked flask fitted with a Hershberg stirrer sealed by a lubricated rubber sleeve, a dropping funnel, and a reflux condenser attached to a calcium chloride drying tube are placed 46.5 g. (0.86 mole) of sodium methoxide (Note 1) and 1 l. of ether (dried over sodium wire). The flask is cooled in an ice bath, and a mixture of 46.4 g. (0.8 mole) of acetone (Note 2) and 59.2 g. (0.8 mole) of ethyl formate (Note 3) is added through the dropping funnel at a rate of about 2 drops per second, with stirring, during a period of about 1 hour. Stirring is continued 15 minutes longer with the ice bath in place and then 1 hour after it is removed. The reflux condenser is replaced by a condenser set for distillation, and the ether is distilled by heating the mixture in a water bath at a temperature which is not allowed to rise above 70°. Stirring is continued as long as possible during the distillation. The last of the ether is removed by distillation under reduced pressure with the aid of a water aspirator (Note 4).

To the solid residue of sodium formylacetone remaining in the flask are added a solution of 67 g. (0.8 mole) of cyanoacetamide

t-Butyl Hypochlorite

WARNING

It has been reported [C. P. C. Bradshaw and A. Nechvatal, *Proc. Chem. Soc.*, 213 (1963)] that, during the preparation of *t*-butyl hypochlorite according to these directions an explosion occurred causing moderate physical damage and minor injury to the operator. The cause of the accident has been attributed to lack of proper temperature control during addition of chlorine. It is strongly recommended that the reaction vessel be fitted with a thermometer that dips into the reaction mixture and that the rate of flow of chlorine be regulated so that the temperature of the reaction mixture never exceeds 20°.

Please insert this sheet opposite page 32 of *Org. Syntheses*, **32** (1952), and page 125 of *Org. Syntheses*, Coll. Vol. **4** (1963).

(Note 5) in 400 ml. of water and piperidine acetate (prepared by adding piperidine to 8 ml. of glacial acetic acid in 20 ml. of water until the solution is just basic to litmus). The flask is equipped with a reflux condenser, and the mixture is heated under reflux for 2 hours. At the end of this time 200 ml. of water is added, and the solution is acidified (to litmus) with acetic acid, causing separation of the product as a voluminous yellow precipitate. The mixture is cooled in an ice bath for 2 hours, and the product is collected on a suction filter, washed on the filter with three 100-ml. portions of ice water, and dried (Note 6). The yield of 3-cyano-6-methyl-2(1)-pyridone is 59–67 g. (55–62%); m.p. 292–294° (dec., cor.) (Notes 7, 8, and 9).

2. Notes

1. Commercial sodium methoxide obtained from the Mathieson Alkali Works was used. If the commercial product is not available, sodium methoxide can be prepared by dissolving clean sodium in dry methanol and removing the excess methanol by distillation and finally by heating the residue to 200° under good vacuum furnished by an oil pump (protected by Dry Ice traps).²

2. Reagent grade acetone is dried over potassium carbonate and distilled.

3. Commercial ethyl formate was purified by the procedure described earlier.³

4. If not all the ether is removed, it will be impossible to obtain the reflux temperature needed for the subsequent condensation, in which case the remainder of the ether must be removed by a preliminary distillation after adding the aqueous solution of cyanoacetamide and piperidine acetate.

5. Either Eastman Kodak Company white label grade cyanoacetamide or a product prepared according to the procedure described previously⁴ can be used.

6. The product retains water tenaciously and is best dried in a vacuum oven at 70–100° at a pressure of 30 mm. or lower.

7. Melting points determined in the ordinary way are unsatisfactory because gradual decomposition occurs over a broad tem-

perature range. Reproducible melting points were obtained by placing the sample in a melting-point tube and displacing the air in the tube with nitrogen introduced through a fine capillary (prepared by drawing out a piece of glass tubing, which then was attached to a nitrogen cylinder through a T-tube dipping into 1–2 cm. of mercury). The nitrogen-filled melting-point tube was sealed quickly, and the melting point was determined by placing the tube in a bath 10° below the melting point and raising the temperature 2° per minute.

8. Analysis of the crude product is approximately 0.9% low in carbon. Analytically pure 3-cyano-6-methyl-2(1)-pyridone, m.p. $296.5\text{--}298.5^{\circ}$ (dec., cor., under nitrogen), can be obtained by one recrystallization from 50% (by volume) ethanol, using 66 ml. per g. of product and treating the hot solution with Darco. Recovery of the product is 60%, and concentration of the mother liquor yields impure material.

9. A similar procedure can be used for preparing other 2(1)-pyridones. For example, 3-cyano-6-isobutyl-2(1)-pyridone can be obtained from the sodium salt of formylmethyl isobutyl ketone, and 3-cyano-5,6-dimethyl-2(1)-pyridone can be prepared from the sodium salt of α -formylethyl methyl ketone.⁵

3. Methods of Preparation

The procedure used for preparing the sodium salt of formylacetone is a modification of a previously described procedure.² 3-Cyano-6-methyl-2(1)-pyridone has been prepared by the condensation of β -ethoxycrotonaldehyde diethyl acetal with cyanoacetamide⁶ and by condensation of the sodium salt of formylacetone with cyanoacetamide.⁷

¹ Northwestern University, Evanston, Illinois.

² Johnson, Woroch, and Mathews, *J. Am. Chem. Soc.*, **69**, 570 (1947).

³ *Org. Syntheses* Coll. Vol. **2**, 180 (1943).

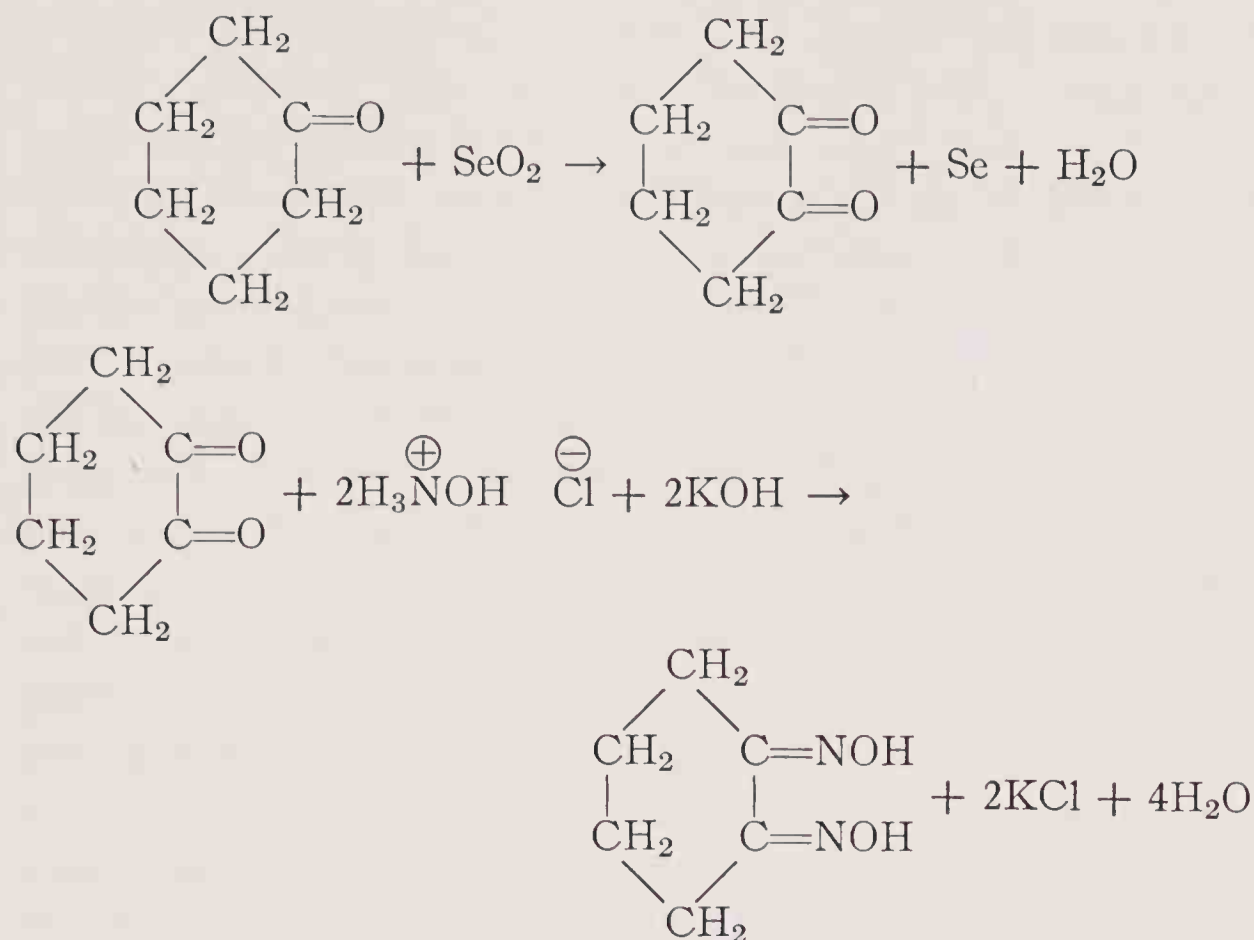
⁴ *Org. Syntheses* Coll. Vol. **1**, 179 (1941).

⁵ Mariella, *J. Am. Chem. Soc.*, **69**, 2670 (1947).

⁶ Dornow, *Ber.*, **73B**, 153 (1940).

⁷ Perez-Medina, Mariella, and McElvain, *J. Am. Chem. Soc.*, **69**, 2574 (1947).

1,2-CYCLOHEXANEDIONEDIOXIME



Submitted by CLIFFORD C. HACH, CHARLES V. BANKS, and HARVEY DIEHL.¹
 Checked by R. T. ARNOLD and PHILIP N. GORDON.

1. Procedure

A. *1,2-Cyclohexanedione*. A 3-l. round-bottomed flask, fitted with stirrer and dropping funnel, is placed in a water bath containing a copper coil through which cooling water may be circulated. In the 3-l. flask is placed 1708 g. (15.2 moles, 1.8 l.) of cyclohexanone (Note 1). Tap water is circulated through the cooling coil (Note 2), and a solution containing 387 g. (3 moles) of selenious acid (H_2SeO_3) (Note 3), 500 ml. of dioxane, and 100 ml. of water is added dropwise and with stirring to the cyclohexanone over a period of 3 hours. The reaction mixture immediately turns yellow, and red amorphous selenium gradually appears. Stirring is continued for 5 additional hours at water-bath temperatures and then for 6 more hours at room temperature.

Removal of the bulky, amorphous selenium is accomplished with the aid of a 6-in. Büchner funnel. The selenium is returned to the reaction flask and extracted with 300 ml. of boiling 95% ethanol for 1 hour (Note 4). The solution, obtained by decantation from the compact gray selenium, is combined with the above filtrate in a 4-l. distilling flask. Distillation under reduced pressure gives two fractions. The lower-boiling fraction (25–60°/16 mm.) consists mainly of ethanol, water, dioxane, and cyclohexanone; the higher-boiling one (60–90°/16 mm.) contains cyclohexanone and 1,2-cyclohexanedione with traces of water and dioxane. The yield of crude product is approximately 322 g.

The higher-boiling fraction is redistilled (Note 5), and again two fractions, boiling at 25–75°/16 mm. and 75–79°/16 mm., are collected. The latter fraction is essentially pure 1,2-cyclohexanedione and crystallizes at 34° to ice-like crystals which become light yellow-green when exposed to the air; yield 202.5 g. (63% based on selenous acid). A considerable amount of light-brown, clear, resinous residue remains in the distilling flask.

B. *1,2-Cyclohexanedionedioxime*. In a 1-l. Erlenmeyer flask is placed 200 ml. of water and 100 g. of cracked ice. To this ice-water mixture is added 86.9 g. (1.25 moles) of hydroxylammonium chloride. An ice-cold basic solution is prepared by dissolving 70.1 g. (1.25 moles) of potassium hydroxide in 50 ml. of water and then adding 150 g. of cracked ice. The ice-cold potassium hydroxide solution is added to the hydroxylammonium chloride solution, and the mixture is thoroughly shaken. To the mixture is added about 0.5 g. of nioxime (1,2-cyclohexanedionedioxime) with stirring (Note 6). The solution turns red owing to the reaction of the nioxime with quantities of iron and other impurities in the reagents. Four grams of Norit is added; the mixture is thoroughly shaken and then filtered with the aid of a 5-in. Büchner funnel. After this operation the filtrate should be water white.

The cold solution is transferred to a 1-l. Erlenmeyer flask and is placed in an ice bath. To the stirred solution is added slowly 56 g. (0.5 mole) of melted 1,2-cyclohexanedione. Precipitation of the 1,2-cyclohexanedionedioxime should take place almost im-

mediately. If not, the solution may be seeded to initiate rapid precipitation. The mixture is stirred for 30 minutes after the addition of the 1,2-cyclohexanedione, and the precipitate is then collected on a 5-in. Büchner funnel. The precipitate is thoroughly washed with water to remove inorganic salts. The 1,2-cyclohexanedionedioxime is partially dried by suction and finally dried in a vacuum desiccator to give snow-white crystals; yield 52.5 g. (74%); m.p. 185–188° (darkening at 170°) (Note 7). The crude 1,2-cyclohexanedionedioxime is recrystallized from 550 ml. of water using 2.5 g. of iron-free Norit; yield 39.3 g. (55%); m.p. 186–188°.

2. Notes

1. The cyclohexanone need not be freshly distilled. Commercial cyclohexanone, obtained from the Barrett Division, Allied Chemical & Dye Corporation, New York, New York, gave practically the same yield as carefully fractionated cyclohexanone.

2. If too much selenous acid is added at once, or the cooling discontinued, the solution will heat up and the reaction will become extremely vigorous with subsequent decrease in yield.

3. Selenous acid or selenium dioxide can apparently be used interchangeably.

4. The selenium filtered from the reaction mixture is refluxed with 3 l. of 95% ethanol for 1 hour, which converts the red amorphous form to the gray hexagonal form and frees it of organic matter. This metallic selenium is removed by filtration, washed with water, and converted to the dioxide by the method of Baker and Maxson.²

5. A distilling head such as J-1104 obtained from Scientific Glass Apparatus Company, Bloomfield, New Jersey, was used.

6. This treatment must obviously be omitted on the first preparation; the product will be light pink rather than snow white, as obtained when the reagents are purified in this manner.

7. This material is 96.5% pure as determined by precipitation of the nickel compound and is satisfactory as an analytical reagent.

3. Methods of Preparation

A. 1,2-Cyclohexanedione has been prepared by brominating cyclohexanone and treating the resulting 2,6-dibromocyclohexanone with aqueous potassium hydroxide to obtain the dihydroxy compound which loses water to yield the dione; ³ by heating divinyl glycol with copper; ⁴ and by oxidizing cyclohexanone with selenium dioxide in an ethanolic solution.^{5, 6}

B. 1,2-Cyclohexanedionedioxime has been prepared by oximating 1,2-cyclohexanedione with hydroxylammonium chloride in aqueous potassium hydroxide solution; ^{3, 6} by oximating 2-isonitrosocyclohexanone with hydroxylammonium chloride; ^{7, 8} and by oximating sodium 2-isonitrosocyclohexanone with hydroxylammonium chloride in methanolic solution.⁶

¹ Iowa State College, Ames, Iowa.

² Booth, *Inorg. Syntheses*, **1**, 119–120 (1939).

³ Wallach and Weissenborn, *Ann.*, **437**, 172 (1924).

⁴ Urion, *Compt. rend.*, **192**, 1662 (1931).

⁵ Riley, Morley, and Friend, *J. Chem. Soc.*, **1932**, 1875.

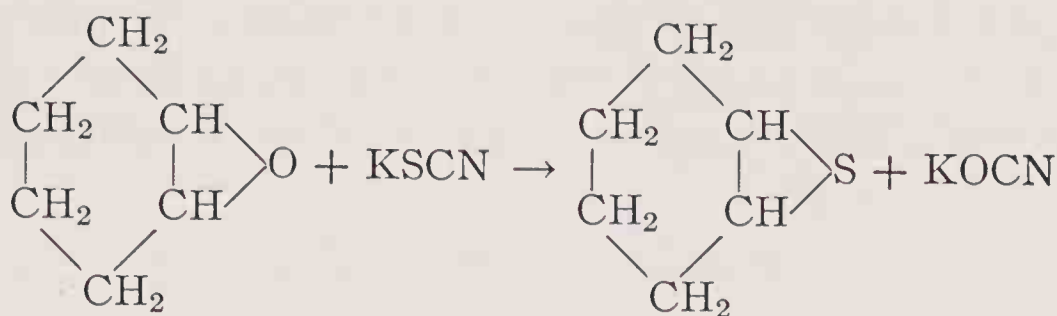
⁶ Rauh, Smith, Banks, and Diehl, *J. Org. Chem.*, **10**, 199 (1945).

⁷ Treibs and Dinelli, *Ann.*, **517**, 160 (1935).

⁸ Jaeger and van Dijk, *Proc. Acad. Sci. Amsterdam*, [1] **39**, 384, 392 (1936).

CYCLOHEXENE SULFIDE

[7-Thiabicyclo (4,1,0) heptane]

Submitted by EUGENE E. VAN TAMELEN.¹

Checked by CHARLES C. PRICE and PAUL F. KIRK.

1. Procedure

Ninety-eight grams (1 mole) of cyclohexene oxide (Note 1) is divided into two approximately equal portions; one portion is added to a solution of 121 g. (1.25 moles) of potassium thiocyanate in 100 ml. of water and 75 ml. of 95% ethanol. After standing for 3–4 hours (Note 2) the clear solution is transferred to a 1-l. flask equipped with a mechanical stirrer. The second portion of oxide is added, and the resulting solution is stirred vigorously for 36 hours at room temperature. The supernatant layer and the aqueous phase are then decanted from the precipitated potassium cyanate into a 1-l. separatory funnel. The potassium cyanate is rinsed with 50 ml. of ether, which is subsequently added to the separatory funnel and used to extract the cyclohexene sulfide. The ether extract is washed twice with 50-ml. portions of saturated sodium chloride solution and then dried over anhydrous sodium sulfate. The excess ether is removed on the steam bath, and the residual liquid is distilled under reduced pressure through an 18-in. Vigreux column while the distillate is being cooled in ice. The main fraction boils at 71.5–73.5°/21 mm. (69–71°/19 mm.) (Note 3); n_D^{25} 1.5306–1.5311. A fore-run, boiling up to 71.5°/21 mm., yields more of the product on redistillation. The total yield of cyclohexene sulfide is 81.5–83.5 g. (71–73%).

2. Notes

1. The cyclohexene oxide (b.p. 129–134°) was prepared from 2-chlorocyclohexanol.²
2. During this time a temperature rise of about 5° occurs.
3. Cyclohexene sulfide can be stored at about 5° in a closed container for at least a month without apparent decomposition.

3. Methods of Preparation

Cyclohexene sulfide has been prepared by the action of thio-urea, potassium thiocyanate, or ammonium thiocyanate on cyclohexene oxide.³ The method described above is a modification of that of Snyder, Stewart, and Ziegler.⁴

¹ University of Wisconsin, Madison, Wisconsin.

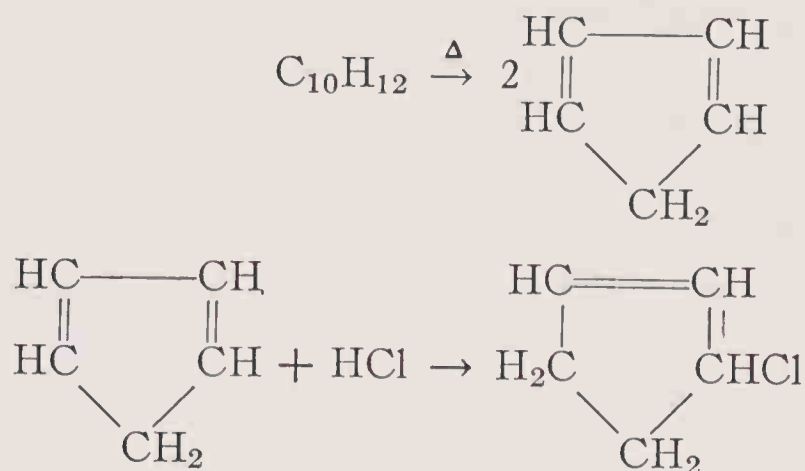
² *Org. Syntheses* Coll. Vol. 1, 179 (1932).

³ Culvenor, Davies, and Pausacker, *J. Chem. Soc.*, **1946**, 1050.

⁴ Snyder, Stewart, and Ziegler, *J. Am. Chem. Soc.*, **69**, 2672 (1947).

CYCLOPENTADIENE AND 3-CHLOROCYCLOPENTENE

(Cyclopentene, 3-chloro-)

Submitted by ROBERT BRUCE MOFFETT.¹

Checked by R. T. ARNOLD and GEORGE P. SCOTT.

1. Procedure

A. *Cyclopentadiene*. Two hundred milliliters (195 g.) of technical dicyclopentadiene (Note 1) is placed in a 500-ml. two-necked round-bottomed flask equipped with thermometer and an upright Friedrichs-type condenser (through which water at 50° (Note 2) is circulated). The ground-glass (Note 3) outlet of the Friedrichs condenser is connected to the side arm of a simple distilling head fitted with a thermometer and attached to an efficient water-cooled condenser held in a vertical position. At the lower end of this condenser is a receiver which consists of a carefully weighed 500-ml. two-necked round-bottomed flask immersed in a Dry Ice bath (Note 4) and protected from the air by a calcium chloride drying tube.

The flask containing dicyclopentadiene is now heated by means of an electric heating mantle or oil bath to approximately 160°, or until cyclopentadiene distils smoothly at 38–46° and a little dicyclopentadiene refluxes from the cold-finger (Friedrichs) condenser. After two-thirds of the dicyclopentadiene has been pyrolyzed (during the course of 4–5 hours), the residue in the flask may tend to become viscous and a higher temperature for

the pyrolysis will be required in order to obtain rapid distillation of cyclopentadiene. In such an event it is desirable to discard the residue while it is still hot and mobile.

Cyclopentadiene dimerizes rapidly at room temperature and should be used immediately (Note 5) or stored at Dry Ice temperatures. As obtained above, the product has a refractive index of about 1.433 at 25° and is quite satisfactory as a starting material for the following preparation (Note 6). The yield, which is determined by weighing the receiving flask plus product, depends upon the quality of dicyclopentadiene employed (Note 7).

B. *3-Chlorocyclopentene*. The flask containing cyclopentadiene is weighed and the quantity of cyclopentadiene determined (Note 8). A thermometer and gas inlet tube are passed through a two-holed rubber stopper which is fitted to the center neck of the flask; the side neck is fitted with a calcium chloride drying tube. While the flask containing cyclopentadiene is being cooled in a Dry Ice bath (Note 9), dry hydrogen chloride (Note 10) is passed in rapidly. During this operation the temperature of the reaction mixture must be kept below 0° and the flask swirled to ensure good mixing. From time to time the flask is detached, wiped dry, and weighed quickly in order to determine the amount of hydrogen chloride that has been added. An excess is to be avoided, and it is advisable to stop the addition about 10% short of the theoretical quantity.

For many purposes, this crude 3-chlorocyclopentene, either as such or in solution (Note 5), may be used without purification (Notes 11 and 12). If a purer product is desired, however, it may be distilled according to the following procedure.

The flask containing the crude product is equipped with a capillary tube and distilling head and surrounded by a water bath, which may be heated by a hot plate or steam cone. A water-cooled condenser connects the distilling head with the center neck of a two-necked receiver which is surrounded by a Dry Ice bath. The outer neck of the receiver is fitted with a Dry Ice condenser arranged in such a way that vapors which

first escape the receiver are condensed and returned to it. This apparatus is connected through a second Dry Ice trap and soda-lime tower (Note 13) to a vacuum pump. A fore-run is removed at a bath temperature of 20° and a pressure of about 15 mm. The receiver is changed, and the product is distilled at 18–25°/5 mm. The temperature of the water bath should not exceed 30°. 3-Chlorocyclopentene is obtained as a colorless liquid in a yield of 70–90% based on cyclopentadiene; n_D^{26} 1.4708.

2. Notes

1. Coarse iron filings or turnings may be added to speed up the rate of depolymerization,² but they are of questionable value.

2. Water at 50° may be obtained by carefully mixing streams from hot and cold water taps. A more elegant method is to circulate water from a thermostatically controlled constant-temperature bath.

3. It is desirable to use ground-glass jointed equipment throughout.

4. An ice-salt bath may be used but is not so effective. A very convenient fluid for use in Dry Ice baths is ethylene glycol monomethyl ether (methyl cellosolve, Carbide and Carbon Chemicals Corporation, New York, New York).

5. If the cyclopentadiene is to be used in solution, it is convenient to collect it directly in a flask containing a weighed amount of the desired solvent (e.g., toluene or ether).

6. Further purification, if desired, may be accomplished by distillation at about 20 mm. while collecting the product in a Dry Ice cooled receiver.

7. The checkers used Eastman Kodak Company blue label dicyclopentadiene and obtained yields approximating 87%.

8. This reaction should be carried out with undiluted cyclopentadiene if reasonably pure distilled 3-chlorocyclopentene is to be isolated. However, if a distilled product is not required, a solution of cyclopentadiene (Note 5) may be used. 3-Chlorocyclopentene is somewhat more stable in solution.

9. If Dry Ice is not available, an ice-salt bath may be used but then the hydrogen chloride must be added at a much slower rate.

10. Hydrogen chloride gas from a cylinder is most convenient; however, it may be generated if desired.²

11. If the temperature has been kept sufficiently low and an excess of hydrogen chloride avoided, the product will be a clear (or only slightly turbid) colorless, mobile liquid. If an excess of hydrogen chloride seems to be present, or if the product is dark, distillation is advisable.

12. 3-Chlorocyclopentene is unstable at room temperature and soon polymerizes to a black tar which is very difficult to remove from the apparatus. It should be used at once or stored at temperatures well below 0°. All apparatus must be cleaned as soon as possible after completion of the experiment. Ground-glass joints, if not separated soon after the reaction is completed, may become cemented together.

13. In spite of the Dry Ice cooled trap and soda-lime tower, some low-boiling material (as evidenced by the odor) often reaches the pump. It is therefore recommended that an old pump be used and the oil changed immediately after the experiment.

3. Methods of Preparation

The only practical laboratory preparation of cyclopentadiene is by the depolymerization of dicyclopentadiene.^{3, 4, 5, 6} 3-Chlorocyclopentene has been prepared by the addition of hydrogen chloride to cyclopentadiene.^{2, 7, 8, 9, 10}

¹ The Upjohn Company, Kalamazoo, Michigan.

² *Org. Syntheses* Coll. Vol. 1, 293, 534 (1941).

³ Perkins and Cruz, *J. Am. Chem. Soc.*, **49**, 518 (1927).

⁴ Stobbe and Reuss, *Ann.*, **391**, 151 (1912).

⁵ Khambata and Wasserman, *Nature*, **138**, 368 (1936).

⁶ Ward, U. S. pat. 2,372,237 [*C. A.*, **39**, 3312 (1945)].

⁷ Kraemer and Spilker, *Ber.*, **29**, 552 (1896).

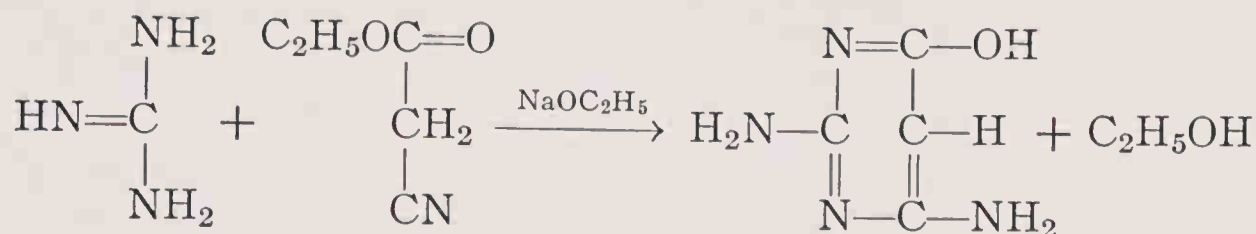
⁸ Noeldechen, *Ber.*, **33**, 3348 (1900).

⁹ Noller and Adams, *J. Am. Chem. Soc.*, **48**, 2444 (1926).

¹⁰ Buu-Hoi and Cagniant, *Bull. soc. chim. France*, [5] **9**, 99 (1942).

2,4-DIAMINO-6-HYDROXYPYRIMIDINE

(4-Pyrimidol, 2,6-diamino-)

Submitted by J. A. VANALLAN.¹

Checked by CLIFF S. HAMILTON and JOHN D. SCULLEY.

1. Procedure

A solution of sodium ethoxide is prepared from 23 g. (1 gram atom) of sodium and 250 ml. of anhydrous ethanol in a 1-l. round-bottomed flask fitted with a reflux condenser carrying a calcium chloride drying tube. After the sodium has dissolved, the solution is cooled and 113 g. (1 mole) of ethyl cyanoacetate is added (Note 1). This mixture is allowed to stand while a second solution of sodium ethoxide of the same volume and concentration is prepared. To this solution is added 97 g. (1.02 moles) of guanidine hydrochloride. The sodium chloride is separated by filtration, and the clear filtrate containing guanidine is added to the solution of ethyl sodiocyanoacetate. This mixture is heated for 2 hours under reflux and is then evaporated to dryness at atmospheric pressure. The solid product is dissolved in 325 ml. of boiling water and acidified with 67 ml. of glacial acetic acid. Upon cooling of the solution, 101–103 g. (80–81%) of yellow needles separates; m.p. 260–270° (dec.) (Note 2).

2. Notes

1. Eastman Kodak Company white label grade of ethyl cyanoacetate was used by the checkers.

2. Analyses carried out by the checkers showed that the product is quite pure.

3. Methods of Preparation

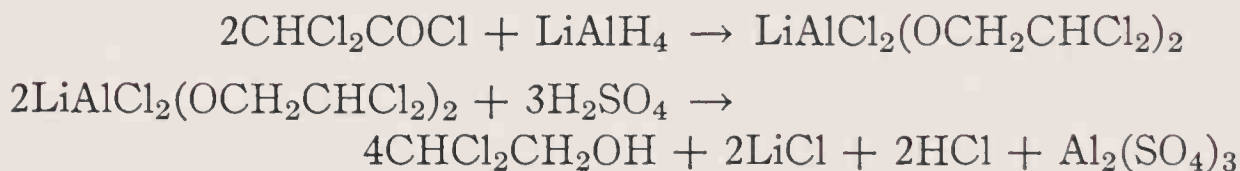
The procedure is a modification of the method of Traube.²

¹ Eastman Kodak Company, Rochester, New York.

² Traube, *Ber.*, **33**, 1371 (1900); Ger. pat. 135,371 [*Frdl.*, **6**, 1192 (1900-1902)].

2,2-DICHLOROETHANOL

(Ethanol, 2,2-dichloro-)



Submitted by C. E. SROOG and H. M. WOODBURN.¹

Checked by R. S. SCHREIBER and C. J. LINTNER, JR.

1. Procedure

Caution! This procedure should be carried out in a good hood, and a spark-proof motor should be used.

A 1-l. three-necked flask having ground-glass joints is fitted with an efficient reflux condenser, a dropping funnel, and a mercury-sealed stirrer, and all exits are protected by drying tubes (Note 1). In the flask are placed 300 ml. of rigorously dried ether (Note 2) and 13.6 g. (0.36 mole) of pulverized lithium aluminum hydride (Note 3). After the mixture has been stirred for 15 minutes, a milky suspension is produced. A solution of 88.6 g. (0.60 mole) of dichloroacetyl chloride in 75 ml. of dry ether is added from the dropping funnel (Note 4) at a rate such as to produce gentle reflux. The process is completed in about 2.5 hours (Note 5).

Agitation is continued for 30 minutes after all the chloride has been introduced, and the excess hydride is then destroyed by the careful, dropwise addition of water to the stirred and cooled reaction mixture. The hydrolysis is accompanied by the formation of a white curdy mass of aluminum hydroxide, and

the mixture has a semisolid consistency when the hydride has been completely decomposed (Note 6). With constant stirring, 500 ml. of 10% sulfuric acid is then added slowly to the mass. Stirring is continued for 30 minutes, and the solution becomes clear during this period.

The ether layer is separated, and the solvent is removed by distillation under atmospheric pressure, and the dark-colored residue is fractionated under reduced pressure through a 25-cm. column packed with glass helices. The fraction boiling at 37–38.5°/6 mm. is collected; it weighs 44–45 g. (63–65%); n_D^{25} 1.4626; d_4^{25} 1.404 (Note 7).

2. Notes

1. To prevent partial hydrolysis of the lithium aluminum hydride, the checkers found it desirable to dry the glassware by flaming while dry nitrogen was being swept through the apparatus.

2. Anhydrous ether is recommended since a solvent containing moisture will react to coat the hydride with oxides which will retard its rate of solution. The checkers used ether dried over sodium wire.

3. The hydride can be pulverized rapidly and safely by breaking the large pieces with a spatula, followed by careful crushing with a mortar and pestle.

4. The acid chloride was obtained from the Eastman Kodak Company and was used without prior treatment. The submitters report that dichloroacetic acid or ethyl dichloroacetate may be substituted for dichloroacetyl chloride but that the reaction appears to be smoother with the acid chloride.

5. The acid chloride should be added slowly since the reaction appears to have a short induction period and it is undesirable to accumulate a large quantity of unreacted material.

6. The decomposition of the hydride is accompanied by the vigorous evolution of hydrogen. Cessation of hydrogen formation is evidence that the hydride is completely decomposed.

7. The following constants have been reported in the literature for 2,2-dichloroethanol: d_4^{15} 1.415; d_4^{19} 1.416; $n_D^{17.3}$ 1.4752.³

3. Methods of Preparation

2,2-Dichloroethanol has been prepared by the reaction of dichloroacetaldehyde with zinc dialkyls² and aluminum alkoxides.³

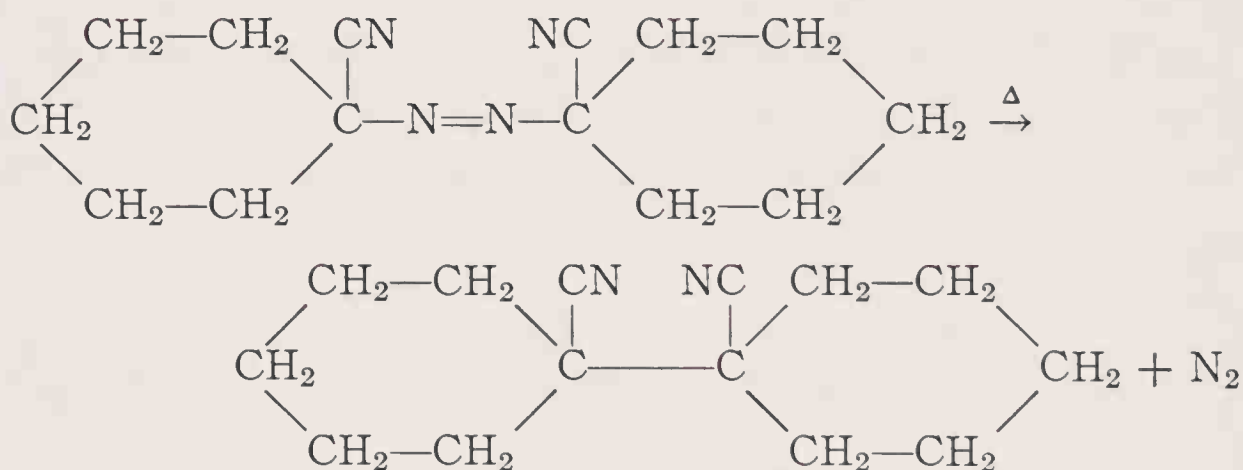
¹ University of Buffalo, Buffalo, New York.

² de Lacre, *Compt. rend.*, **104**, 1184 (1887).

³ Boeseken, Tellegen, and Plusje, *Rec. trav. chim.*, **57**, 73 (1938).

1,1'-DICYANO-1,1'-BICYCLOHEXYL

([Bicyclohexyl]-1,1'-dicarbonitrile)



Submitted by C. G. OVERBERGER and M. B. BERENBAUM.¹

Checked by N. J. LEONARD and E. H. MOTTUS.

1. Procedure

In a 200-ml. flask equipped with a reflux condenser are placed 20 g. (0.082 mole) of 1,1'-azo-*bis*-1-cyclohexanenitrile (p. 16) and 50 ml. of toluene. The solution is heated under gentle reflux for 8 hours, and the reaction mixture is placed in a refrigerator overnight. The product is collected on a Büchner funnel and air-dried; yield 11.5–12.2 g. (65–69%); m.p. 224.5–225.5° (Note 1).

2. Notes

1. Tetramethylsuccinonitrile can be prepared from 2,2'-azo-*bis*-isobutyronitrile in a similar manner.² In this case petroleum

ether (b.p. 60–70°) is added to the reaction mixture before cooling it overnight. The yield is 75–81% of the theoretical amount; m.p. 168–170°. Sublimation at 20–50 mm. raises the melting point to 170.5–171.5° with very little loss of material.

3. Methods of Preparation

1,1'-Dicyano-1,1'-bicyclohexyl has been prepared previously by Hartman³ in a similar manner. The procedure has been substantiated by Overberger, O'Shaughnessy, and Shalit.⁴

¹ Polytechnic Institute of Brooklyn, Brooklyn, New York.

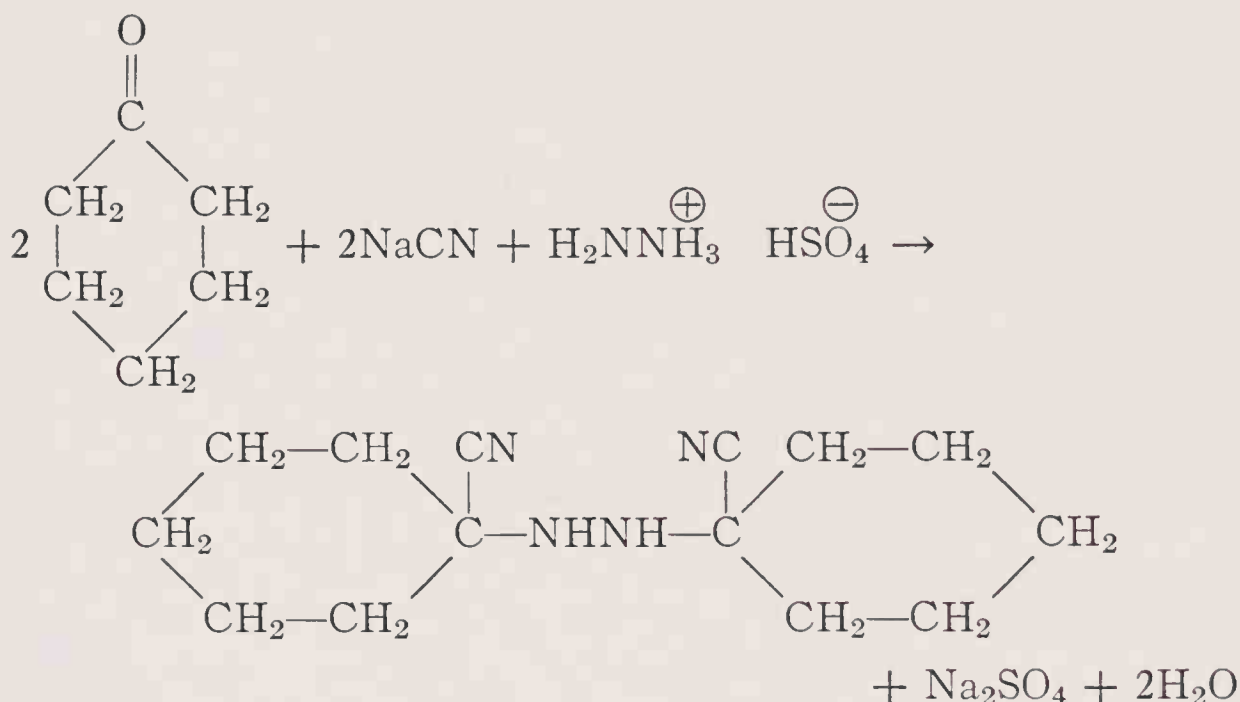
² Thiele and Heuser, *Ann.*, **290**, 1 (1896).

³ Hartman, *Rec. trav. chim.*, **46**, 150 (1927).

⁴ Overberger, O'Shaughnessy, and Shalit, *J. Am. Chem. Soc.*, **71**, 2661 (1949).

1,2-DI-1-(1-CYANO)-CYCLOHEXYLHYDRAZINE

(Cyclohexanecarbonitrile, 1,1'-hydrazodi-)

Submitted by C. G. OVERBERGER, PAO-TUNG HUANG, and M. B. BERENBAUM.¹

Checked by N. J. LEONARD and E. H. MOTTUS.

1. Procedure

Caution! These operations should be conducted in an efficient hood.

In a 600-ml. screw-capped bottle are placed 15.4 g. (0.314 mole) of sodium cyanide, 20.5 g. (0.158 mole) of hydrazine sulfate (Note 1), and 400 ml. of ice water. The bottle is capped to prevent loss of hydrogen cyanide (Note 2) and held in an ice bath for 15 minutes. To the cooled mixture is added 29.4 g. (0.3 mole) of cyclohexanone. The bottle is recapped and cooled for an additional 15 minutes. The bottle is then shaken intermittently over a period of 6 hours and allowed to stand an additional 14 hours. The bottle is cooled again before opening. The suspension is filtered by means of suction, and the cake is washed thoroughly with 250 ml. of ice water. After the crude product has been pressed dry on the filter (Note 3), it is transferred to a

500-ml. Erlenmeyer flask and 150 ml. of boiling 95% ethanol is added. The suspension is brought into solution as rapidly as possible by warming on a hot plate (Note 4) and is filtered quickly through a prewarmed 7.5-cm. Büchner funnel. An additional 10 ml. of hot 95% ethanol is used to dissolve any organic residue on the filter, and the combined filtrates are warmed to redissolve any precipitate. The solution is allowed to stand undisturbed for 6 hours in an icebox. The product is collected on a Büchner funnel, washed with 15 ml. of cold 95% ethanol, and then dried over solid calcium chloride in a vacuum desiccator. The yield of product is 24.5–26 g. (66–70%); m.p. 147–149° (Note 5).

2. Notes

1. Technical hydrazine sulfate of known purity is suitable.
2. Both hydrazine and hydrogen cyanide are toxic, and appropriate precautions should be taken.
3. The checkers have used the dry, crude product directly in the conversion to 1,1'-azo-*bis*-1-cyclohexanenitrile (see p. 16) with an over-all yield of 72% based upon cyclohexanone.
4. Excessive or prolonged heating will result in a decreased yield owing to decomposition of the product.
5. 1,2-Di-2-(2-cyano)propylhydrazine (2,2'-hydrazo-*bis*-isobutyronitrile) may be prepared in a similar manner from acetone. The crude product (m.p. 89–91°; yield 88–93%) can be oxidized directly to 2,2'-azo-*bis*-isobutyronitrile. The dried impure material can be recrystallized from ether; m.p. 91.5–92.5°; (72–77%).

3. Methods of Preparation

1,2-Di-1-(1-cyano)-cyclohexylhydrazine has been prepared by a procedure similar to that used by Hartman.² The procedure has been substantiated by Overberger, O'Shaughnessy, and Shalit.³

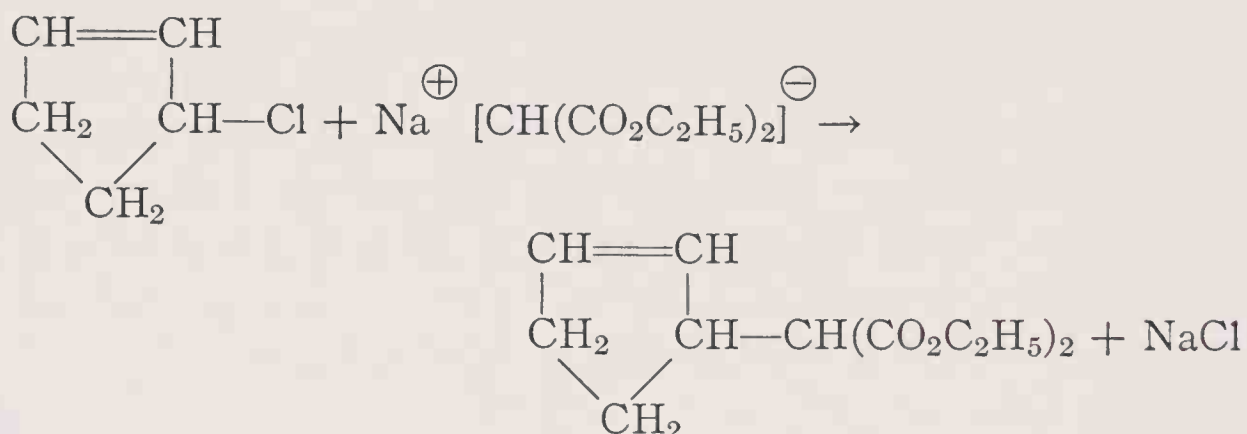
¹ Polytechnic Institute of Brooklyn, Brooklyn, New York.

² Hartman, *Rec. trav. chim.*, **46**, 150 (1927).

³ Overberger, O'Shaughnessy, and Shalit, *J. Am. Chem. Soc.*, **71**, 2661 (1949).

DIETHYL Δ^2 -CYCLOPENTENYLMALONATE

(2-Cyclopentene-1-malonic acid, diethyl ester)

Submitted by ROBERT BRUCE MOFFETT.¹

Checked by R. T. ARNOLD and GEORGE P. SCOTT.

1. Procedure

Nine hundred and twenty-five milliliters of absolute ethanol (Note 1) is placed in a 2-l. three-necked round-bottomed flask, fitted with a mercury or glycerin-sealed stirrer (Note 2), dropping funnel, and reflux condenser. To this is added 46 g. (2 gram atoms)² of freshly cut sodium, a few pieces at a time and at such a rate that the reaction proceeds rapidly but the solvent does not reflux too vigorously. When most of the sodium has dissolved, a calcium chloride drying tube is fitted to the top of the condenser and 320 g. (2 moles) of redistilled diethyl malonate is added from the dropping funnel. Then 205 g. (2 moles) of 3-chlorocyclopentene (p. 42) (Note 3) is added at such a rate that a gentle reflux is maintained. Towards the end of the addition, it is desirable to test the reaction mixture with *pH* test paper, and the addition should be stopped if the solution becomes acidic.

When the addition is complete, the condenser is set downward for distillation, the stirring is continued, and most of the ethanol is removed by distillation on a steam bath (Note 4). After cooling, the reaction mixture is diluted with sufficient water to dissolve the salt, and the layers are separated. The

aqueous layer is extracted with 50 ml. of ether. The ethereal solution is added to the ester, and the resulting solution is washed with saturated salt solution and dried over anhydrous magnesium sulfate. The ethereal solution is transferred to a Claisen flask, the solvent is evaporated, and the product is distilled under reduced pressure. The fraction boiling at about 85–140°/12 mm. is collected and redistilled through an efficient fractionating column (Note 5). The product distils at 130°/12 mm. (Note 6). The yield is about 276.5 g. (61%); n_D^{20} 1.4536.

2. Notes

1. The preparation of absolute ethanol has been described earlier.³

2. The glycerin-sealed stirrer has been described earlier.²

3. It is not necessary to use redistilled 3-chlorocyclopentene; however, if large amounts of impurities are present, difficulty may be encountered in obtaining a pure product.

4. If a glycerin-sealed stirrer is used, the rate of solvent evaporation may be accelerated by means of gentle water-pump suction.

5. Careful fractionation is necessary in order to secure a pure product. The submitter used a 12-in. column packed with 1/8-in. glass helices. The fore-run should be redistilled to separate any ester it may contain.

6. Other boiling points are 140°/18 mm.; 97°/1 mm.

3. Methods of Preparation

Diethyl Δ^2 -cyclopentenylmalonate has been prepared by the alkylation of malonic ester with 3-chlorocyclopentene.^{4, 5, 6, 7, 8}

¹ The Upjohn Company, Kalamazoo, Michigan.

² *Org. Syntheses*, **21**, 40 (1941).

³ *Org. Syntheses Coll. Vol. 1*, 259 (1941).

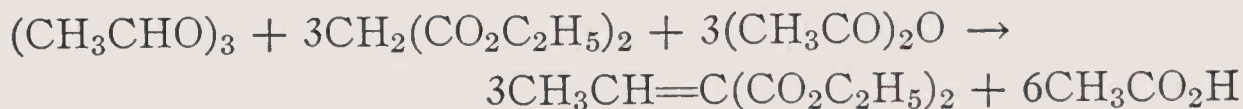
⁴ Noller and Adams, *J. Am. Chem. Soc.*, **48**, 2444 (1926).

⁵ Perkins and Cruz, *J. Am. Chem. Soc.*, **49**, 518 (1927).

⁶ Wagner-Jauregg and Arnold, *Ann.*, **529**, 274 (1937).

⁷ Horclois, *Chimie & industrie*, **31**, 357 (Special No., April, 1934).

⁸ Buu-Hoi and Cagniant, *Bull. soc. chim. France*, [5] **9**, 99 (1942).

DIETHYL ETHYLIDENEMALONATE**(Malonic acid, ethylidene-, diethyl ester)**Submitted by WILLIAM S. FONES.¹

Checked by ARTHUR C. COPE, HARRIS E. PETREE, and E. R. TRUMBULL.

1. Procedure

In a 1-l. three-necked flask, equipped with a thermometer and a reflux condenser, are placed 60 g. of paraldehyde (0.45 mole, equivalent to 1.35 moles of acetaldehyde) and 100 ml. (1.06 moles) of acetic anhydride. Ice water is circulated through the condenser, and the reaction mixture is protected from atmospheric moisture by a drying tube containing Drierite. The temperature of the mixture is raised slowly by heating with an electric mantle to 125°, at which point gentle refluxing begins. Then 100 g. (0.62 mole) of diethyl malonate is added in 15-ml. portions at a rate of 1 portion every 30 minutes. During the addition of diethyl malonate, the temperature gradually drops to about 100°, and the mixture is heated so as to maintain a reflux rate of 30–60 drops per minute. After the addition is complete, the reaction mixture is heated under reflux for 4 hours at the specified rate.

The reflux condenser is replaced by a Claisen distillation head, and the reaction mixture is distilled until the temperature of the vapor reaches 140°. The residue is transferred to a smaller flask and fractionated through a 30-cm. column packed with glass helices. A low-boiling fraction containing ethylidene diacetate and diethyl malonate is collected first, followed by 79–89.5 g. (68–77%) of diethyl ethylidenemalonate; b.p. 102–106°/10 mm.; n_D^{25} 1.4394 (Note 1).

2. Notes

1. The submitters obtained a yield of 70% when three times the above quantities were used, in which case the diethyl malonate was added at a rate of 90 ml. per hour.

3. Methods of Preparation

Diethyl ethylidenemalonate has been prepared by heating acetaldehyde, diethyl malonate, and acetic anhydride;^{2,3} by heating the same reagents plus zinc chloride;⁴ by treating acetaldehyde and diethyl malonate with sodium ethoxide or piperidine;⁵ and by heating diethyl malonate, ethylidene bromide, and ethanolic sodium ethoxide.⁶

¹ National Institutes of Health, Bethesda, Maryland.

² Komnenos, *Ann.*, **218**, 157 (1883).

³ Goss, Ingold, and Thorp, *J. Chem. Soc.*, **123**, 3353 (1923).

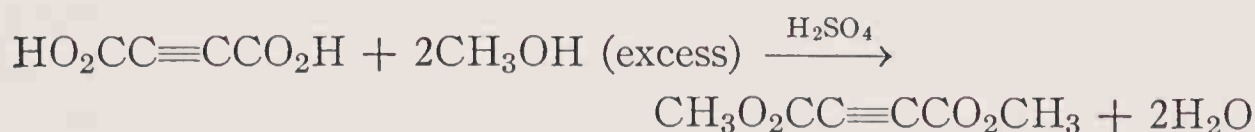
⁴ von Auwers and Eisenlohr, *J. prakt. Chem.*, [2] **84**, 101 (1911).

⁵ Higginbotham and Lapworth, *J. Chem. Soc.*, **123**, 1622 (1923).

⁶ Loevenich, Losen, and Dierichs, *Ber.*, **60**, 957 (1927).

DIMETHYL ACETYLENEDICARBOXYLATE

(Acetylenedicarboxylic acid, dimethyl ester)



Submitted by E. H. HUNTRESS, T. E. LESSLIE, and J. BORNSTEIN.¹

Checked by T. L. CAIRNS and M. J. HOGSED.

1. Procedure

To 400 g. (510 ml., 12.5 moles) of methanol (commercial grade) in a 2-l. round-bottomed flask is added in small portions with cooling 200 g. (111 ml., 2.04 moles) of concentrated sulfuric

acid. To this cooled solution is added 100 g. (0.66 mole) of the potassium acid salt of acetylenedicarboxylic acid (Note 1). The flask is fitted with a stopper holding a calcium chloride drying tube and allowed to stand with occasional swirling for 4 days at room temperature.

The liquid in the flask is then decanted from the inorganic salt, which is washed with 500 ml. of cold water. The solutions are combined and extracted with five 500-ml. portions of ether. The ether extracts are combined and washed successively with 200 ml. of cold water, 150 ml. of saturated sodium bicarbonate solution (Note 2), and 200 ml. of cold water and then dried over anhydrous calcium chloride. After removal of the ether by distillation from a steam bath, the ester is distilled under reduced pressure from a modified Claisen flask. The yield of ester boiling at 95–98°/19 mm. is 67–82 g. (72–88%) (Notes 3 and 4); n_D^{25} 1.4444–1.4452.

2. Notes

1. The potassium acid salt of acetylenedicarboxylic acid is commercially obtainable from the National Aniline Division, Allied Chemical and Dye Corporation, New York, New York. Directions for the preparation of the free acid are given in earlier volumes.^{2, 3}

2. If the ether extract is not washed with sodium bicarbonate solution, considerable loss occurs during the distillation of the ester because of decomposition in the flask.

3. Dimethyl acetylenedicarboxylate is a powerful lachrymator and vesicant; it should be handled with extreme care. Even traces of ester on the skin should be washed off at once with 95% ethanol followed by washing with soap and water.

4. The same general method has been used by the submitters to prepare diethyl acetylenedicarboxylate. In this case absolute ethanol was used, and the ether extract was dried over anhydrous magnesium sulfate. The yield of diethyl ester from 100 g. of the acid potassium salt of acetylenedicarboxylic acid was 57–59 g. (51–53%); b.p. 96–98°/8 mm.; n_D^{25} 1.4397.

3. Methods of Preparation

Dimethyl acetylenedicarboxylate has been prepared by refluxing the acid potassium salt of acetylenedicarboxylic acid with methanol and sulfuric acid.^{4,5} The method described here is a substantial improvement over the method of Moureu and Bongrand,⁶ who prepared it from acetylenedicarboxylic acid, absolute methanol, and sulfuric acid.

¹ Massachusetts Institute of Technology, Cambridge, Massachusetts.

² *Org. Syntheses* Coll. Vol. 2, 10 (1943).

³ *Org. Syntheses*, 18, 3 (1938).

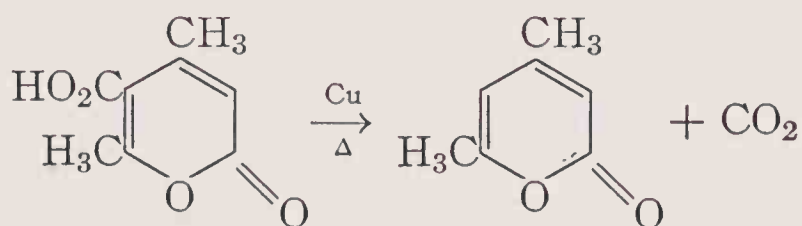
⁴ Baudrowski, *Ber.*, 15, 2694 (1882).

⁵ Curtius and Heynemann, *J. prakt. Chem.*, [2] 91, 66 (1915).

⁶ Moureu and Bongrand, *Ann. chim.*, [9] 14, 11 (1920).

4,6-DIMETHYLCOUMALIN

(Sorbic acid, δ -hydroxy- β -methyl, δ -lactone)



Submitted by NEWTON R. SMITH and RICHARD H. WILEY.^{1,2}

Checked by R. S. SCHREIBER and H. H. FALL.

1. Procedure

In a 125-ml. Claisen flask, equipped with a capillary for vacuum distillation and a thermometer, are placed 50 g. (0.3 mole) of isodehydroacetic acid (p. 76) and 2 g. of copper powder (Note 1). A 125-ml. simple distilling flask, cooled by a water jet, is used as a vacuum receiver and is attached to a water aspirator. The Claisen flask is heated at atmospheric pressure in an oil bath at 230–235° for 45 minutes or until the decarboxylation has ceased. The pressure on the system is then slowly reduced, and

the dimethylcoumalin is distilled directly from the reaction flask (Note 2). The crude dimethylcoumalin (34–35 g., 92–95%) is redistilled from a Claisen flask. The yield of 4,6-dimethylcoumalin is 30–32 g. (81–87%); b.p. 140–142°/35 mm. (Note 3); m.p. 50–51°.

2. Notes

1. Copper chromite catalyst may be substituted.
2. The submitters recommend 3 hours for decarboxylation. At 45-minute intervals the pressure on the system is reduced and the dimethylcoumalin distilled directly from the reaction flask. After the distillation slackens, the pressure is returned to atmospheric and the decarboxylation is continued. However, the checkers found that the decarboxylation is virtually completed during the first 45-minute period.
3. The checkers observed a boiling point of 134–136°/35 mm. for 4,6-dimethylcoumalin. The melting point, however, was identical with that reported by the submitters.

3. Methods of Preparation

4,6-Dimethylcoumalin has been prepared by the decarboxylation of isodehydroacetic acid in sulfuric acid or by heating.³

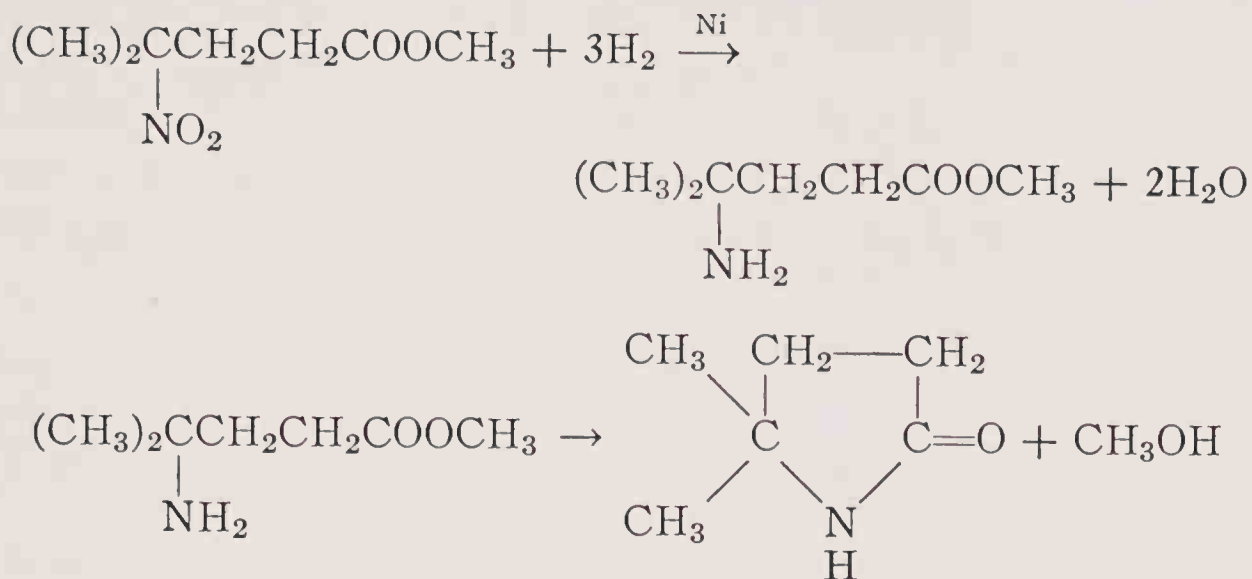
¹ University of Louisville, Louisville, Kentucky.

² The submitters wish to thank the Research Corporation for a grant under which this work was done.

³ Hantzsch, *Ann.*, **222**, 17 (1883).

5,5-DIMETHYL-2-PYRROLIDONE

(2-Pyrrolidone, 5,5-dimethyl-)

Submitted by R. B. MOFFETT.¹

Checked by N. J. LEONARD, W. E. SMITH, and B. L. RYDER.

1. Procedure

To a solution of 148 g. (0.845 mole) of methyl γ -methyl- γ -nitrovalerate (p. 86) in 500 ml. of commercial absolute ethanol (total volume about 632 ml.) in a 2.5-l. rocking high-pressure bomb is added 12.5–25.0 g. (Note 1) of W-5² Raney nickel catalyst (Note 2), previously rinsed with absolute ethanol. The bomb head and fittings are placed in position, including a thermocouple attached to a semi-automatic heating control (Micromax). Hydrogen is introduced into the bomb until the pressure reaches 1000 lb. per sq. in. (Note 3).

The bomb is rocked and the temperature of the solution is raised carefully to 55° during the course of 0.5–1.0 hour (Note 4). The hydrogen uptake begins at 40–51°, and during the reaction period the temperature is held at 55–60°. The rate of pressure drop is 50–100 lb. per sq. in. each 15 minutes. The rocking of the bomb is continued, and the temperature is maintained at 60° until the pressure reading is constant for 1 hour, in order to ensure completion of the reaction.

After the bomb has been cooled the contents are removed and allowed to stand until the catalyst has settled (Note 5). The mixture is filtered, and the filtrate is transferred to a Claisen flask placed in an oil bath. The solvent is removed by distillation at atmospheric pressure, and the oil-bath temperature is raised to 200°. After temporary cooling, the residue in the flask is distilled under reduced pressure. The 5,5-dimethyl-2-pyrrolidone boils at 126.5–128.5°/12 mm. and solidifies in the receiver. The yield is 84–92 g. (88–96%); m.p. 42–43° (Note 6).

2. Notes

1. It is unnecessary and may in fact be dangerous to use a larger amount of catalyst.

2. The checkers have found that commercial grade Raney nickel (Gilman Paint and Varnish Company) is a satisfactory substitute for W-5 catalyst. The yields obtained with the two catalysts are identical, but the hydrogenation requires 2–3 hours with commercial catalyst compared with 1–1.5 hours for W-5 catalyst.

3. The theoretically required drop in hydrogen pressure for a free space of 1868 ml. and equivalent to 2.535 moles of hydrogen is 507 lb. per sq. in. The theoretical pressure drop will vary with the free space when bombs of different capacity are used. The observed pressure drop usually exceeds the theoretical by about 10%.

4. Since batches of Raney nickel may vary in activity, caution must be exercised during the heating period. The temperature should not exceed 60° at any time.

5. Filtration through Hiflo Super-Cel (Johns-Manville Company) speeds the operation but lowers the final yield.

6. The product can be recrystallized from petroleum ether (b.p. 30–38°).

3. Methods of Preparation

5,5-Dimethyl-2-pyrrolidone has been prepared by the hydrolysis of 5-imino-2,2-dimethylpyrrolidine in the presence of Raney

nickel³ or by the hydrogenation of 5-amino-2,2-dimethylpyrroline-N-oxide in the presence of Raney nickel.³ The preparation by this method has not been reported previously.

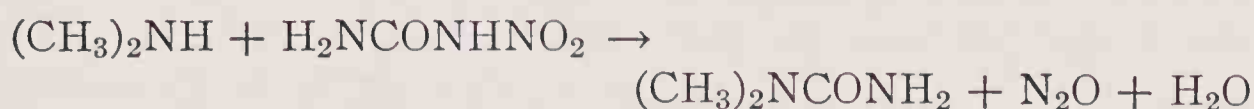
¹ The Upjohn Company, Kalamazoo, Michigan.

² Adkins and Billica, *J. Am. Chem. Soc.*, **70**, 695 (1948).

³ Buckley and Elliott, *J. Chem. Soc.*, **1947**, 1508.

asym-DIMETHYLUREA

(Urea, 1,1-dimethyl-)



Submitted by FREDERICK KURZER.¹

Checked by WILLIAM S. JOHNSON and WILLIAM T. TSATSOS.

1. Procedure

In a 1.5-l. beaker (Note 1), 191 ml. (180 g.) of aqueous 25% dimethylamine solution (1.0 mole) is diluted with 64 ml. of water and treated with 116 g. (1.1 moles) of nitrourea.² The temperature of the resulting brownish liquid rises spontaneously to 35–42°. The solution is warmed to 56–60°, and a reaction sets in vigorously with evolution of nitrous oxide. External cooling with water is applied when required; the reaction temperature is maintained below 70° during the first 5–7 minutes and below 85° during the second period of 5–7 minutes. After a total of 10–15 minutes, the effervescence slackens and the reaction mixture is kept at 90–100° until the evolution of gas has completely ceased. This usually requires an additional 15–20 minutes.

The resulting liquid is heated with about 1 g. of activated carbon and is filtered with suction while hot; the clear, faintly colored filtrate is transferred to an evaporating dish and heated on a steam bath to remove most of the water. The residual, somewhat viscous, liquid (about 120 ml.) is then transferred to a beaker; the evaporating dish is rinsed with 10 ml. of water, and

this solution is added to the contents of the beaker. To this is added 95% ethanol (50 ml.), and the mixture is warmed to effect solution. On cooling, large crystals separate which, at 0°, almost fill the bulk of the solution. The crystalline mass is broken up with a glass rod, collected on a suction filter, and washed quickly, while on the filter, with two successive portions of ice water (Note 2), drained, and air-dried (Note 3). The yield of large, colorless prismatic crystals of *asym*-dimethylurea is 35–40 g. (40–45%); m.p. 182–184° (Note 4).

The combined filtrates, on further evaporation and dilution with 95% ethanol as above, yield an additional 15–20 g. of material of approximately the same quality, bringing the total yield up to 57–68%. In a series of preparations, yields can be further increased a few per cent by carrying over mother liquors to subsequent batches.

2. Notes

1. The reaction mixture froths considerably in the initial stages, and the use of a sufficiently large reaction vessel is important.

2. Since *asym*-dimethylurea is appreciably soluble in water, enough ice water is added to just cover the crystals on the filter, and suction is applied immediately.

3. A slight odor of dimethylamine, which persists, disappears when the product is dried at 80° for 1–2 hours.

4. The use of nitrourea is generally applicable to the preparation of urea derivatives and usually affords the required carbamide in excellent yield.^{3, 4}

3. Methods of Preparation

asym-Dimethylurea has been prepared by the interaction of dimethylamine sulfate and potassium cyanate⁵ or dimethylamine and nitrourea.³ It is also obtained by the hydrolysis of dimethylcyanamide in acid⁶ and alkaline⁷ media. Other reactions yielding the product include the action of dimethylamine on methyl γ -methylallophanate⁸ or diethoxymethyleneimine,⁹

and the hydrolysis of 1,1,2-trimethylisourea¹⁰ or methyl dimethylthiocarbamate.¹¹

¹ School of Medicine, University of London.

² *Org. Syntheses* Coll. Vol. **1**, 417 (1941).

³ Davis and Blanchard, *J. Am. Chem. Soc.*, **51**, 1798 (1929).

⁴ Buck and Ferry, *J. Am. Chem. Soc.*, **58**, 854 (1936).

⁵ Franchimont, *Rec. trav. chim.*, **2**, 122 (1883); **3**, 222 (1884).

⁶ Diels and Gollmann, *Ber.*, **44**, 3165 (1911).

⁷ von Braun and Röver, *Ber.*, **36**, 1197 (1903).

⁸ Biltz and Jeltsch, *Ber.*, **56**, 1920 (1923).

⁹ Schenck, *Arch. Pharm.*, **249**, 467 (1911); *Z. physiol. Chem.*, **77**, 368 (1912).

¹⁰ McKee, *Am. Chem. J.*, **42**, 25 (1909).

¹¹ Delepine and Schving, *Bull. soc. chim. France*, [4] **7**, 900 (1910).

α,α' -DIPHENYLSUCCINONITRILE

(Succinonitrile, α,β -diphenyl-)



Submitted by J. A. MCRAE and R. A. B. BANNARD.¹

Checked by R. T. ARNOLD and STUART W. FENTON.

1. Procedure

Caution! This preparation should be conducted in a good hood.

Two hundred and five grams (1 mole) of α -phenylcinnamionitrile,² 2250 ml. of methanol, and 750 ml. of ether are placed in a 5-l. round-bottomed flask fitted with a two-necked adapter supporting a 1-l. separatory funnel and reflux condenser. The α -phenylcinnamionitrile is dissolved by gentle heating, and the solution is heated under reflux. A solution of 274 g. (4 moles) of 95% potassium cyanide in 600 ml. of water (which has been preheated to 45°) is added rapidly from the separatory funnel (Note 1). A small amount of potassium cyanide precipitates. The solution is heated under reflux for 1 hour, after which a solution of 154 g. (2 moles) of ammonium acetate in 250 ml. of water is added rapidly from the separatory funnel (Note 2).

Heating is discontinued, and the mixture is allowed to stand for 24 hours. The slightly orange-yellow crystalline product is collected on a Büchner funnel and washed, first with two 300-ml. portions of water at 60° to remove inorganic salts, then with 800 ml. of 70% methanol for removal of water and some unreacted α -phenylcinnamionitrile, and finally with two 300-ml. portions of ether for further drying. The colorless needles thus obtained consist of a mixture of the stereoisomeric α,α' -diphenylsuccinonitriles and, after drying at room temperature for 6 hours, weigh 213–218 g. (92–94%). This mixture of stereoisomers melts over a 1–2° range in the region of 202–206° (Note 3).

The mixed dinitrile can be recrystallized from glacial acetic acid (using 27 ml. per g.) to give pure *meso*- α,α' -diphenylsuccinonitrile. Residual acetic acid is removed readily by washing the crystalline product with small portions of water, aqueous methanol (70%), and ether; yield 95–98% (based on mixed dinitrile); m.p. 240–241.5° (cor.).

2. Notes

1. Care must be exercised to avoid superheating of the solution before addition of the cyanide; otherwise ether and α -phenylcinnamionitrile will be lost through the condenser. Superheating can be avoided by adding a boiling chip periodically as the solution approaches its boiling point. No difficulty with superheating occurs after the cyanide has been added.

2. Addition of the ammonium acetate solution may be omitted; the yield is then 203–208 g. (87.5–89.6%).

3. The mixture of dinitriles has been reported to melt over a 1–2° range in the region of 206–221°.³ Analysis of a sample of the mixture of dinitriles produced by the present method showed that no impurities are present.

3. Methods of Preparation

A mixture of the stereoisomeric α,α' -diphenylsuccinonitriles has been obtained by the interaction of benzyl cyanide, benzal

chloride, and potassium cyanide in aqueous ethanolic solutions; ³ by warming α -phenylcinnamionitrile with excess potassium cyanide in aqueous ethanolic solution with, ⁴ or without, ^{5, 6} subsequent addition of dilute acetic acid; by heating under reflux an aqueous ethanolic solution of α -phenylcinnamionitrile and excess potassium cyanide with subsequent addition of saturated ammonium or magnesium chloride solution; ⁷ by the action of sunlight on a mixture of benzyl cyanide and benzophenone; ⁸ and by treatment of benzyl cyanide with sodium methylate and ethereal iodine solution.⁹ The method described here is a modification of Lapworth and McRae's procedure.⁴

¹ Queens University, Kingston, Ontario, Canada.

² *Org. Syntheses*, **29**, 83 (1949).

³ Chalanay and Knoevenagel, *Ber.*, **25**, 289 (1892).

⁴ Lapworth and McRae, *J. Chem. Soc.*, **121**, 1699 (1922).

⁵ Lapworth, *J. Chem. Soc.*, **83**, 995 (1903).

⁶ Knoevenagel and Schleussner, *Ber.*, **37**, 4067 (1904).

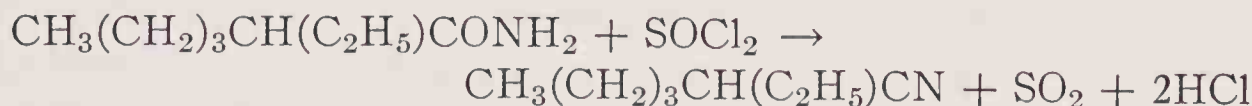
⁷ I. G. Farbenind., A.-G., Ger. pat. 427,416 [*Chem. Centr.*, [2] **97**, 1100 (1926)].

⁸ Paterno, *Gazz. chim. ital.*, **44**, 237 (1914).

⁹ Heller, *J. prakt. Chem.*, **120**, 193 (1929).

2-ETHYLHEXANONITRILE

(Capronitrile, α -ethyl)



Submitted by JOHN A. KRYNITSKY and HOMER W. CARHART.¹

Checked by H. R. SNYDER and RICHARD S. COLGROVE.

1. Procedure

In a 1-l. round-bottomed flask, bearing an efficient reflux condenser (Note 1), are placed 286 g. (2 moles) of 2-ethylhexanamide (Note 2), 300 ml. of dry benzene (Note 3), and 357 g. (218 ml., 3 moles) of thionyl chloride (Note 4). The flask is placed in a water bath, which is heated quickly to 75–80° and maintained at that temperature for 4.5 hours (Note 5). The reaction mixture is transferred to a 1.5-l. beaker and cooled in

an ice bath. A mixture of 100 g. of crushed ice and 100 ml. of water is added to decompose the excess thionyl chloride. Cold 50% potassium hydroxide solution is added in small portions, with stirring, until the mixture is alkaline to litmus (Note 6). The mixture is transferred to a separatory funnel, and the layers are separated. The aqueous portion is extracted with 100 ml. of benzene. The benzene solutions are combined and washed once with 150 ml. of 1% sodium carbonate solution and twice with 150-ml. portions of water (Note 7). The mixture is distilled from a modified Claisen flask, the bulk of the solvent being removed at atmospheric pressure. The yield of nitrile is 215–236 g. (86–94%); b.p. 118–120°/100 mm. (Notes 8, 9, and 10).

2. Notes

1. Unless the temperature of the water supplied to the condenser is below 20°, a larger amount of thionyl chloride may be required. The condenser should be attached to a gas trap.

2. The 2-ethylhexanamide was prepared in 86–88% yield from technical 2-ethylhexanoic acid (Carbide and Carbon Chemicals Corporation) by a method similar to that described previously,² except that the crude amide was filtered directly from the reaction mixture, washed well with water, and dried. The resulting product, which melted at 99–101°, was used without further purification. If the pure amide is desired, this product may be recrystallized (with 83–90% recovery) from 50% ethanol. For 100 g. of amide, 2 l. of 50% ethanol is used, and the hot solution is decolorized with charcoal. The product thus obtained is in the form of white needles which melt at 102–103°.

3. Benzene dried over sodium was used.

4. The submitters used Eastman Kodak Company white label thionyl chloride. The checkers purified commercial thionyl chloride (Hooker Electrochemical Company, refined grade) by the method of Cottle.³

5. It is advisable to carry out the reaction in a hood, as hydrogen chloride and sulfur dioxide are evolved. The evolution of gases stops just before the end of the specified heating period.

6. Approximately 150–200 ml. of the potassium hydroxide solution is required.

7. Drying of the solution is unnecessary, since the water present is removed in the next step by azeotropic distillation with benzene.

8. The checkers collected the product at 70.5–72°/10 mm.; n_D^{25} 1.4145.

9. Benzonitrile also can be prepared by this method in comparable yields, but a longer reaction time (7 hours) is required. The method was found to be unsatisfactory for the preparation of the nitriles of azelaic and phthalic acids from the corresponding diamides.

10. The submitters prepared palmitonitrile in more than 90% yield by heating the amide with a benzene solution of thionyl chloride for 6 hours followed directly by distillation. The nitrile so obtained was contaminated with a product having a strong sulfurous odor which could be removed by washing with aqueous mercuric acetate. By the described procedure, palmitonitrile free from objectionable odor was prepared in 80% yield. Troublesome emulsions were formed during the neutralization and washing steps; the addition of a small amount of ethanol aided in breaking the emulsions.

3. Methods of Preparation

Racemic 2-ethylhexanonitrile has been obtained only by the action of phosphorus pentachloride on 2-ethylhexanaldoxime; ⁴ the levorotatory form has been prepared from the active amide by the method described.⁵ Other amides have been converted to nitriles by dehydration with thionyl chloride.^{5, 6}

¹ Naval Research Laboratory, Washington, D. C.

² *Org. Syntheses*, **25**, 58 (1945).

³ Cottle, *J. Am. Chem. Soc.*, **68**, 1380 (1946).

⁴ von Braun and Manz, *Ber.*, **67**, 1696 (1934).

⁵ Levene and Kuna, *J. Biol. Chem.*, **140**, 263 (1941).

⁶ Michaelis and Siebert, *Ann.*, **274**, 312 (1893).

ETHYL ORTHOCARBONATE

(Orthocarbonic acid, tetraethyl ester)



Submitted by JOHN D. ROBERTS and ROBERT E. MCMAHON.¹

Checked by WILLIAM S. JOHNSON and WILLIAM E. LOEB.

1. Procedure

Caution! This preparation should be conducted in a hood to avoid exposure to chloropicrin.

A solution of sodium ethoxide is prepared under nitrogen from 70 g. (3.04 gram atoms) of sodium and 2-l. of absolute ethanol (Note 1) in a 3-l. three-necked flask which is equipped with mechanical stirrer, efficient reflux condenser, dropping funnel, and a thermometer which dips below the level of the liquid in the flask. Chloropicrin (100 g., 0.61 mole) (Note 2) is placed in the dropping funnel, and the stirred solution is heated to 58–60° with a water bath. The chloropicrin is added at a rate of 30–35 drops per minute until the reaction becomes self-sustaining (about 20 minutes), at which point the water bath is removed and the balance of the chloropicrin is added at a rate sufficient to maintain the temperature at 58–60° (Note 3). When the addition, which requires nearly 2 hours, is complete, the stirrer is stopped and the mixture is allowed to stand overnight.

The flask is connected to a 2 by 50 cm. Vigreux column equipped with a total-reflux partial take-off head, and all but about 400 ml. of the ethanol is removed at 200 mm. pressure with a reflux ratio greater than 5:1 (Note 4).

The residue is cooled, diluted with 1.2 l. of water, and transferred to a 2-l. separatory funnel. The organic layer is separated, washed with 200 ml. of saturated salt solution, and dried over anhydrous magnesium sulfate. The aqueous layer is extracted with a total of 800 ml. of ether used in several small portions. The ethereal extracts are combined, washed first with 500 ml. of water then with 500 ml. of saturated salt solu-

tion, and finally dried over anhydrous magnesium sulfate. The ether is removed through a 1.8 by 25 cm. glass-helix-packed fractionating column with a total-reflux partial take-off head. The residue is combined with the balance of the crude product and distilled through the fractionating column at atmospheric pressure. The yield of ethyl orthocarbonate is 54–57.5 g. (46–49%); b.p. 158–161°; n_D^{25} 1.3905–1.3908.

2. Notes

1. The absolute ethanol was a good commercial grade and contained less than 0.1% of water according to the paraffin-oil test.²

2. Chloropicrin is a skin irritant and a lachrymator. No difficulty was experienced when the preliminary steps were carried out in a good hood.

3. Care should be taken to regulate the temperature and rate of addition of chloropicrin as specified in order to avoid accumulation of unreacted chloropicrin in the reaction mixture during the induction period; otherwise the reaction, which is strongly exothermic, may get out of control.

4. A water bath should be used as a heat source to avoid overheating, which leads to lowered yields. This distillation should be carried out carefully to prevent loss of product by co-distillation with the ethanol.

3. Methods of Preparation

The above procedure is essentially that of Tieckelmann and Post.³ Ethyl orthocarbonate has been prepared by the reaction of chloropicrin and sodium ethoxide by Bassett⁴ and Röse.⁵ Thiocarbonyl perchloride has been reported^{3,6} to react with sodium ethoxide to give good yields of ethyl orthocarbonate.

¹ Massachusetts Institute of Technology, Cambridge, Massachusetts.

² Robertson, *Laboratory Practice of Organic Chemistry*, p. 177, The Macmillan Company, New York, 1943.

³ Tieckelmann and Post, *J. Org. Chem.*, **13**, 265 (1948).

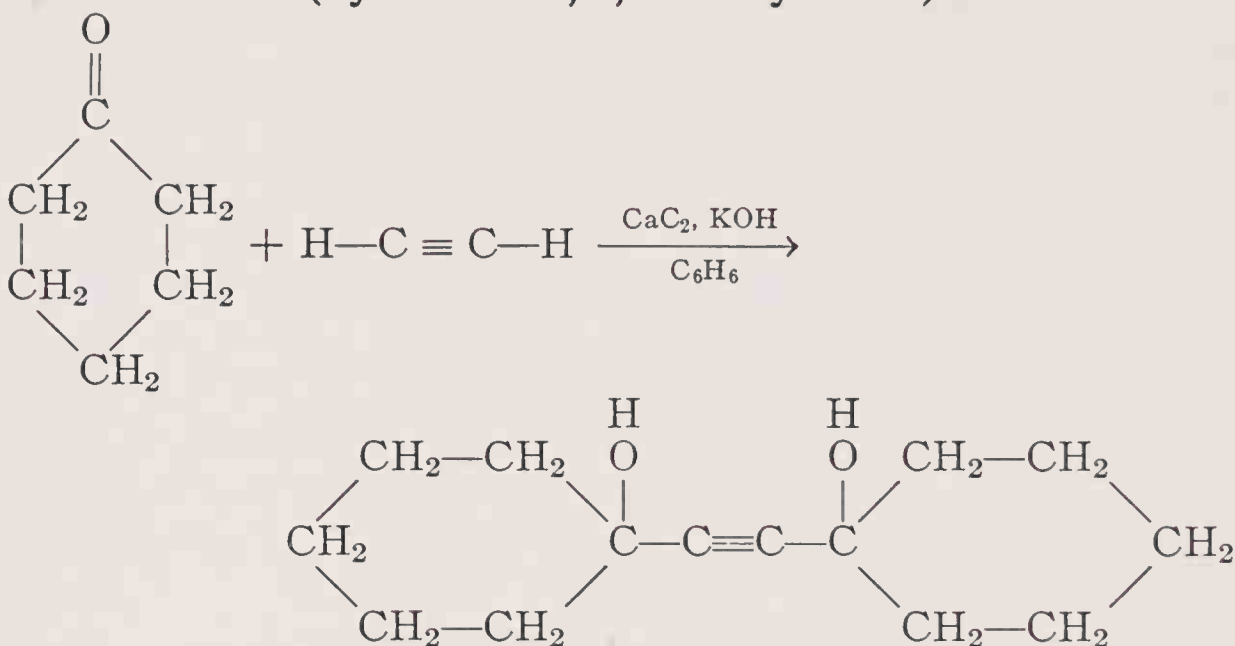
⁴ Bassett, *Ann.*, **132**, 54 (1864).

⁵ Röse, *Ann.*, **205**, 249 (1880).

⁶ Connolly and Dyson, *J. Chem. Soc.*, **1937**, 827.

1,1'-ETHYNYLENE-*bis*-CYCLOHEXANOL

(Cyclohexanol, 1,1'-ethynylenedi-)



Submitted by G. FORREST WOODS and LOUIS H. SCHWARTZMAN.¹
 Checked by RICHARD T. ARNOLD and STUART W. FENTON.

1. Procedure

In a 2-l. three-necked flask (Note 1), fitted with a dropping funnel, condenser (equipped with a Drierite tube), and efficient stirrer driven by a powerful motor, is placed a mixture of 600 ml. of benzene, 48 g. (0.85 mole) of potassium hydroxide (Note 2), and 76.4 g. of powdered calcium carbide (Note 3). While this mixture is being stirred vigorously, 85 g. (0.87 mole) of cyclohexanone is added over a period of 0.5–1 hour. The mixture is dark gray and will become warm, but no external cooling is necessary. Stirring is continued, and within 24 hours the contents congeal (Note 4). This semisolid is allowed to stand for an additional 4 days (Note 5).

The flask is immersed in an ice bath, and a solution containing 200 ml. of concentrated hydrochloric acid and 200 ml. of water is added cautiously (Note 6) over a period of 4–6 hours. The dark solid is separated by filtration with the aid of a large Büchner funnel. This impure product is air-dried and digested with

900 ml. of boiling carbon tetrachloride, and the insoluble portion is collected on a Büchner funnel and subsequently extracted with 100 ml. of hot acetone and again filtered. When the filtrates are kept overnight in a refrigerator, 47.3–50.3 g. (49–52%) of a colorless crystalline product separates; m.p. 106.5–109°. Partial evaporation of the combined filtrates, followed by effective cooling, gives an additional 7.8–12.9 g. (8–13%) of 1,1'-ethynylene-*bis*-cyclohexanol; m.p. 100–109° (Note 7).

2. Notes

1. The submitters employed a 12-l. resin flask equipped with Lightning Stirrer whose shaft and blades were of stainless steel when using 10 times the quantity of starting materials reported here.

Any evolution of acetylene is best accommodated by a rubber tube which leads outside or to a good hood.

2. Either pellets or flakes of potassium hydroxide are powdered in a ball mill.

3. Technical calcium carbide of approximately 100 mesh was obtained from the Union Carbide and Carbon Corporation, New York, New York. The amount of calcium carbide used is in excess and based on an activity of 75%.

4. Stirring is continued until the mass has set solidly; it is desirable for a channel to exist around the stirrer shaft to facilitate the subsequent decomposition.

5. Decreased yields result from shorter periods of standing.

6. It is advisable to bore several holes into the solid mass by means of a stirring rod in order to permit better contact with the acid. Initial addition of the acid should be slow, and a total of 4–6 hours should be allowed for this operation, since considerable heat and acetylene are evolved.

7. The product can be recrystallized from carbon tetrachloride or acetone, or sublimed at reduced pressure, to yield a product melting at 109–111°.

3. Methods of Preparation

This method is based on the procedure of Kazarin.² The same substance has been prepared by the reaction of the dimagnesium halide of acetylene with cyclohexanone³ and also by the reaction of cyclohexanone with acetylene in the presence of potassium *tert*-butoxide followed by the preparation of the Grignard reagent of this compound and further reaction again with cyclohexanone.⁴

¹ University of Maryland, College Park, Maryland.

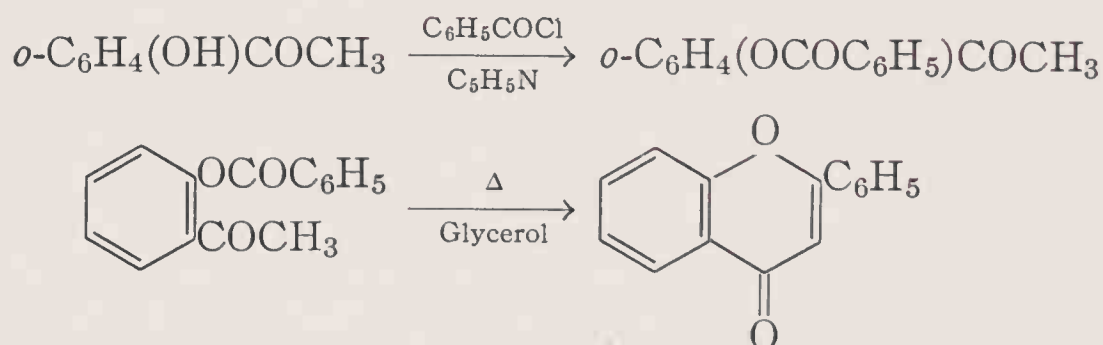
² Kazarin, *J. Gen. Chem. U.S.S.R.*, **4**, 1347 (1934).

³ Dupont, *Ann. chim.*, [8] **30**, 485 (1913).

⁴ Pinkney, Nesty, Wiley, and Marvel, *J. Am. Chem. Soc.*, **58**, 972 (1936).

FLAVONE

Method 1



Submitted by T. S. WHEELER.¹

Checked by R. L. SHRINER and DONALD A. SCOTT.

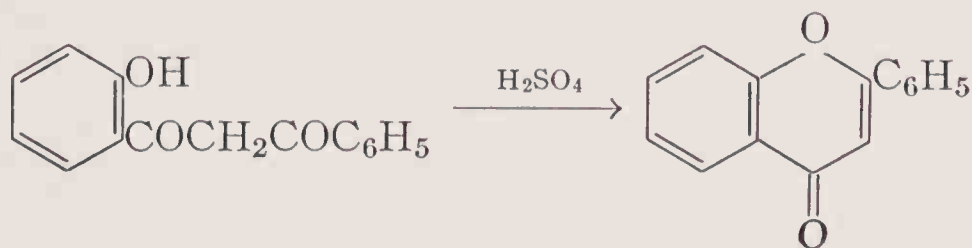
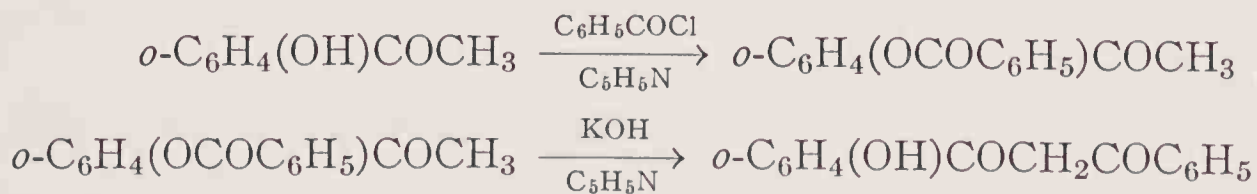
1. Procedure

A. *o*-Benzoyloxyacetophenone. In a 100-ml. conical flask fitted with a calcium chloride drying tube are placed 13.6 g. (12 ml., 0.1 mole) of *o*-hydroxyacetophenone,² 21.1 g. (17.4 ml., 0.15 mole) of benzoyl chloride, and 20 ml. of pyridine (Note 1). The temperature of the reaction mixture rises spontaneously, and when no further heat is evolved (about 15 minutes) the mixture is poured with good stirring into 600 ml. of 3% hydrochloric

acid containing 200 g. of crushed ice. The product is collected on a Büchner funnel and washed with 20 ml. of methanol, then with 20 ml. of water. The product is sucked as dry as possible and air-dried at room temperature. The yield of dry crude product melting at 81–87° is 22–23 g. It is recrystallized from 25 ml. of methanol, and the *o*-benzoyloxyacetophenone is obtained as white crystals; yield 19–20 g. (79–83%); m.p. 87–88°.

B. *Flavone*. In a 500-ml. round-bottomed three-necked flask, equipped with a mercury-sealed mechanical stirrer, a thermometer, and an air condenser closed with a calcium chloride drying tube in the second neck, are placed 20 g. (0.083 mole) of *o*-benzoyloxyacetophenone and 200 ml. of freshly distilled anhydrous glycerol (Note 2). A stream of nitrogen, dried by passage through a wash bottle containing sulfuric acid, is introduced through the third neck. The mixture is heated and maintained at 260° for two hours while being stirred continuously. The contents are cooled below 100° and then poured into 2 l. of water which is rendered slightly alkaline with aqueous sodium hydroxide. The mixture is stirred for 15 minutes, cooled, and kept at 0° (in a refrigerator) for 48 hours. The tan-colored crystals of flavone are collected on a filter and dried at 50°. The yield of crude product amounts to about 10 g.; m.p. 90–93°. The crude material is dissolved in 400 ml. of hot ligroin (b.p. 60–70°). Repeated partial evaporation of the solvent in stages, each followed by cooling, gives successive crops of flavone as white needles. The yield of pure flavone amounts to 8–9 g. (43–48%); m.p. 96–97°.

Method 2



A. *o*-Benzoyloxyacetophenone. This is prepared as in Method 1.

B. *o*-Hydroxydibenzoylmethane. A solution of 20 g. (0.083 mole) of *o*-benzoyloxyacetophenone in 75 ml. of pyridine (Note 1) is prepared in a 300-ml. beaker and warmed to 50°. To the solution is added 7 g. of hot pulverized potassium hydroxide (Note 3), and the mixture is mechanically stirred for 15 minutes, during which time a copious precipitate of the yellow potassium salt of *o*-hydroxydibenzoylmethane forms (Note 4). The mixture is cooled to room temperature and acidified with 100 ml. of 10% acetic acid. The diketone separates as a light-yellow precipitate which is collected on a filter and sucked dry (Note 5). The yield of crude *o*-hydroxydibenzoylmethane is 16–17 g. (80–85%); m.p. 117–120°.

C. *Flavone*. To a solution of 16.6 g. (0.069 mole) of the crude diketone in 90 ml. of glacial acetic acid, contained in a 250-ml. conical flask, is added, with shaking, 3.5 ml. of concentrated sulfuric acid. The mixture is heated under a reflux condenser on a steam bath for 1 hour with occasional shaking and is then poured onto 500 g. of crushed ice with vigorous stirring. After the ice has melted, the crude flavone is collected on a filter, washed with water (about 1 l.) until free from acid, and finally dried at 50°. The yield of product is 14.5–15 g. (94–97%); m.p. 95–97°. The over-all yield of flavone based on *o*-hydroxyacetophenone is 59–68%. The product may be recrystallized from ligroin as in Method 1.

2. Notes

1. Commercial pyridine is dried over solid sodium hydroxide and distilled through a fractionating column.

2. Glycerol is twice distilled under reduced pressure and used immediately in the reaction.

3. The potassium hydroxide is pulverized rapidly in a mortar previously heated at 100°.

4. The mixture usually becomes so thick and pasty that hand stirring is necessary.

5. *o*-Hydroxydibenzoylmethane can be crystallized from 95% ethanol and forms crystals melting at 120°, which give a strong enol reaction with ferric chloride. Crystallization is not necessary here.

3. Methods of Preparation

o-Benzoyloxyacetophenone has been prepared by the action of benzoyl chloride on a pyridine solution of *o*-hydroxyacetophenone.³ The rearrangement of *o*-benzoyloxyacetophenone to *o*-hydroxydibenzoylmethane by alkali has been described.^{4,5} The latter diketone has been made by the base-catalyzed condensation of ethyl benzoate with *o*-hydroxyacetophenone.⁶ The cyclization of *o*-hydroxydibenzoylmethane described in Method 2 is based on the work of Doyle, Gogan, Gowan, Keane, and Wheeler.⁵ Cyclization has also been effected by use of glacial acetic acid containing hydrogen chloride or sodium acetate.⁴

Other methods of preparing flavone include: the action of ethanolic alkali on 2'-acetoxy- α,β -dibromochalcone;⁷ Claisen condensation of ethyl *o*-ethoxybenzoate and acetophenone, and cyclization of the resulting 1,3-diketone with hydriodic acid;⁸ and treatment of 3-bromoflavanone with potassium hydroxide in ethanol.⁹ Flavone has also been prepared from ethyl phenylpropionate by condensation with sodium phenoxide and subsequent cyclization with phosphorus pentachloride in benzene;¹⁰ by fusing *o*-hydroxyacetophenone with benzoic anhydride and sodium benzoate;¹¹ by the dehydrogenation of 2'-hydroxychalcone with selenium dioxide;¹² and by the action of alkali on flavylum chloride.¹³

Method 1 is a new method for the direct production of flavone from *o*-benzoyloxyacetophenone and has been successfully applied to the synthesis of other flavones. Method 2, which involves the Baker-Venkataraman transformation, is recommended because of its high over-all yield and the reproducibility of the results. Mozingo and Adkins' method⁶ is satisfactory but the yield of *o*-hydroxydibenzoylmethane is variable.

¹ University College, Dublin, Ireland.

² *Org. Syntheses* Coll. Vol. 2, 545 (1943); *Org. Syntheses*, 21, 45 (1941).

³ Freudenberg and Orthner, *Ber.*, **55**, 1748 (1922); Baker, *J. Chem. Soc.*, **1933**, 1386.

⁴ Baker, *J. Chem. Soc.*, **1933**, 1386; Bhalla, Mahal, and Venkataraman, *J. Chem. Soc.*, **1935**, 868; Virkar and Wheeler, *J. Chem. Soc.*, **1939**, 1681.

⁵ Doyle, Gogan, Gowan, Keane, and Wheeler, *Sci. Proc. Roy. Dublin Soc.*, **24**, 291 (1948).

⁶ Mozingo and Adkins, *J. Am. Chem. Soc.*, **60**, 672 (1938).

⁷ Feuerstein and Kostanecki, *Ber.*, **31**, 1757 (1898).

⁸ Kostanecki and Tambor, *Ber.*, **33**, 330 (1900).

⁹ Kostanecki and Szabranski, *Ber.*, **37**, 2634 (1904).

¹⁰ Ruhemann, *Ber.*, **46**, 2188 (1913); Bogert and Marcus, *J. Am. Chem. Soc.*, **41**, 87 (1919).

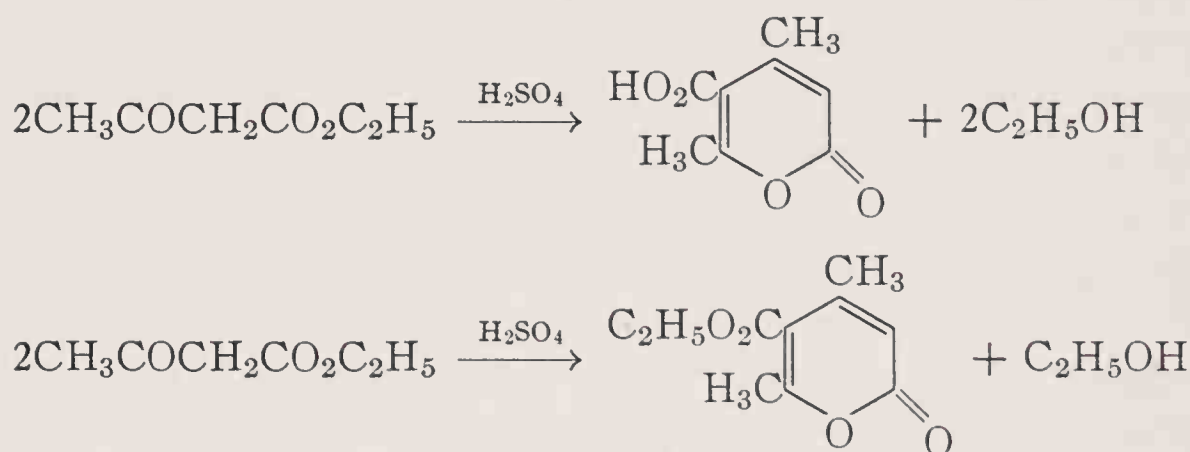
¹¹ Chadha and Venkataraman, *J. Chem. Soc.*, **1933**, 1073.

¹² Mahal, Rai, and Venkataraman, *J. Chem. Soc.*, **1935**, 866.

¹³ Hill and Melhuish, *J. Chem. Soc.*, **1935**, 1165.

ISODEHYDROACETIC ACID AND ETHYL ISODEHYDROACETATE

(Coumalic acid, 4,6-dimethyl- and coumalic acid, 4,6-dimethyl-, ethyl ester)



(Note 1)

Submitted by NEWTON R. SMITH and RICHARD H. WILEY,^{1,2}

Checked by R. S. SCHREIBER and H. H. FALL.

1. Procedure

In a 2-l. three-necked flask fitted with a thermometer, a stirrer, and a dropping funnel is placed 900 ml. of concentrated sulfuric acid. To this solution, cooled in an ice bath, is added, with stirring, 635 ml. (650 g., 5 moles) of ethyl acetoacetate (Note 2) at

such a rate that the temperature remains between 10° and 15°. When all the ester has been added, the flask is stoppered with a calcium chloride drying tube and allowed to stand at room temperature. After 5–6 days (Note 3) the reaction mixture is poured onto 2 kg. of crushed ice while being stirred vigorously with a wooden paddle. The solid is collected on a large Büchner funnel, washed with two 200-ml. portions of cold water, and sucked as dry as possible.

The filtrate, *ca.* 4 l. in volume, is extracted with three 1.5-l. portions of ether (Note 4), and the sulfuric acid mother liquors are discarded. The ether extracts are combined and used to dissolve the solid mixture of acid and ester. If necessary, more ether can be added to assist in dissolving the solid. The ether solution is washed with 50 ml. of cold water and extracted with approximately ten 100-ml. portions of saturated sodium carbonate solution until all the isodehydroacetic acid has been removed (Note 5). The combined sodium carbonate extracts are acidified with an excess of concentrated hydrochloric acid, and the finely divided acid which precipitates is redissolved by heating to the boiling point. The hot solution is filtered with the aid of suction and is cooled in an ice bath; the solid is collected on a filter. The crude isodehydroacetic acid is dissolved in 400 ml. of hot water, and this solution treated with decolorizing carbon, filtered, and cooled slowly to effect crystallization. The yield of isodehydroacetic acid is 91–115 g. (22–27%); m.p. 154–155°.

The ether extract, which contains ethyl isodehydroacetate, is dried for 24 hours over anhydrous sodium sulfate, and the ether is then removed by heating on a water bath. The residue is distilled from a 250-ml. Claisen flask, under reduced pressure, to give 130–175 g. (27–36%) of ethyl isodehydroacetate; b.p. 185–192°/35 mm.; m.p. 18–20° (Notes 6 and 7).

2. Notes

1. Two equations are written since isodehydroacetic acid is not esterified rapidly and its ester is not hydrolyzed rapidly under the conditions used here.

2. The checkers used Eastman Kodak Company white label ethyl acetoacetate as received.

3. If the reaction mixture is allowed to stand only 24 hours, the yields drop about 10% for both the acid and its ester.

4. Occasionally a large amount of carbon dioxide is present in the solution, and caution should be exercised in the extraction with ether.

5. The checkers found it convenient to test the *pH* of the extract with Hydrion papers. When the *pH* of the extract became the same as that of the saturated sodium carbonate solution, the color of the extract changed from green to orange. Thereafter, extraction was continued until neutralization of small aliquots with concentrated hydrochloric acid produced no solid.

6. The fore-run of 30–40 g. consists mostly of a mixture of 4,6-dimethyl-1,2-pyrone and ethyl isodehydroacetate.

7. The ester may be hydrolyzed to the acid by heating on a steam bath with 5 times its weight of concentrated sulfuric acid for 5–8 hours. The yield of acid is 40–50% with about 30% of the original ester recovered.

3. Methods of Preparation

Isodehydroacetic acid has been prepared by the action of sulfuric acid on acetoacetic ester.^{3,4} The ethyl ester has been prepared by the action of dry hydrogen chloride on acetoacetic ester^{5,6} and by the sodium-catalyzed condensation of ethyl β -chloroisocrotonate with ethyl acetoacetate.³ The methyl ester of isodehydroacetic acid has been prepared by the thermal rearrangement of pyrazolines.⁷

¹ University of Louisville, Louisville, Kentucky.

² The submitters wish to thank the Research Corporation for a grant under which this work was done.

³ Anshutz, Bendix, and Kerp, *Ann.*, **259**, 148 (1890).

⁴ Hantzsch, *Ann.*, **222**, 1 (1883).

⁵ Duisberg, *Ber.*, **15**, 1387 (1882).

⁶ Goss, Ingold, and Thorpe, *J. Chem. Soc.*, **123**, 348 (1923).

⁷ Büchner and Schröder, *Ber.*, **35**, 782 (1902).

β -KETOISOÖCTALDEHYDE DIMETHYL ACETAL(Enanthaldehyde, ϵ -methyl- β -oxo-, dimethylacetal)Submitted by CHARLES C. PRICE and JOSEPH A. PAPPALARDO.¹

Checked by R. S. SCHREIBER, WM. BRADLEY REID, JR., and R. W. JACKSON.

1. Procedure

A dry 1-l. three-necked flask fitted with a mercury-sealed stirrer, a calcium chloride drying tube, and a 500-ml. dropping funnel, protected by a calcium chloride drying tube, is surrounded by an ice-salt mixture at -11° . Anhydrous methanol (130 ml.) (Notes 1 and 2) and 161 g. (1 mole) of β -chlorovinyl isoamyl ketone (p. 27) are poured into the flask (Note 3). A solution of 43 g. (1.04 moles) of sodium hydroxide (97%) and 350 ml. of absolute methanol (Note 4) is added dropwise with stirring over a period of 2 hours, during which time the bath temperature is kept between -11° and -8° .

The reaction mixture is poured, with stirring, into 1 kg. of a saturated sodium chloride solution (Note 5). The mixture is extracted with four 100-ml. portions of low-boiling petroleum ether. The extracts are combined and dried over anhydrous potassium carbonate. The liquid is decanted, the potassium carbonate is washed with 25 ml. of low-boiling petroleum ether, and the solution is added to the main fraction. A pinch of anhydrous potassium carbonate is added to the petroleum ether solution, and the solution is then distilled from a Claisen flask to give a colorless liquid; yield 151–169 g. (80–90%); b.p. $122-125^\circ/25$ mm.; n_D^{25} 1.4260; d_4^{25} 0.932 (Note 6).

2. Notes

1. Absolute methanol (C.P. grade) was used.
2. The checkers ran this preparation at one-third the scale described here and obtained equivalent results.
3. When this procedure is used to make the dimethyl acetal of β -ketobutyraldehyde, the methanol and β -chlorovinyl methyl ketone must be mixed quickly and cooled well. If these two liquids are placed in the same flask without immediate cooling and mixing, the ketone may decompose rapidly with the evolution of heat and large amounts of hydrogen chloride.
4. It takes about 1 hour of shaking to dissolve the sodium hydroxide pellets.
5. If this reaction is used to prepare the water-soluble dimethyl acetal of β -ketobutyraldehyde, the product of the reaction is not poured into the saturated sodium chloride solution. Instead, the methanol solution is filtered from the sodium chloride and distilled.
6. The product darkens a little on standing but undergoes no change in refractive index.

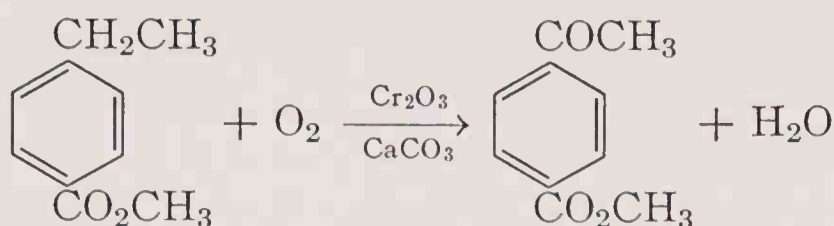
3. Methods of Preparation

The preparation described ² has been used by Nelles ³ to make a variety of β -ketoacetals.

¹ University of Notre Dame, Notre Dame, Indiana.

² Price and Pappalardo, *J. Am. Chem. Soc.*, **72**, 2613 (1950).

³ Nelles, U. S. pat. 2,091,373 [*C. A.*, **31**, 7444 (1937)]; Brit. pat. 466,890 [*C. A.*, **31**, 7886 (1937)].

METHYL *p*-ACETYLBENZOATE(Benzoic acid, *p*-acetyl-, methyl ester)Submitted by WILLIAM S. EMERSON and GEORGE F. DEEBEL.¹

Checked by ARTHUR C. COPE and WARREN N. BAXTER.

1. Procedure

A 200-ml. three-necked flask is equipped with a thermometer, a mechanical stirrer, a gas inlet tube extending as far into the flask as the stirrer permits, and a trap (designed to return the heavier layer of the condensate) (Note 1), which is attached to a bulb and a coil-type reflux condenser connected in series. Methyl *p*-ethylbenzoate (98 g., 0.597 mole) (Note 2) and a mixture of 1 g. of chromium oxide and 4 g. of calcium carbonate, prepared by grinding the solids together in a mortar, are added. An air line with a bleed control valve (Note 3) is connected from the top of the condenser to a water aspirator. The flask is heated with a hemispherical electric mantle (Note 4).

The mixture is stirred vigorously at a temperature of 140–150°, and air is drawn through it (Note 5) for 24 hours while the water formed is collected in the trap (Note 6). At the end of this period, the mixture is cooled, diluted with 100 ml. of benzene (Note 7), and filtered with suction to remove the catalyst (Note 8). The catalyst is washed with 10 ml. of benzene on the funnel, and the washings are combined with the filtrate. The benzene is distilled from the clear, yellow solution (conveniently at a pressure of 100 mm. or lower to avoid superheating and partial decomposition of the product) through a fractionating column (Note 9). After removal of the benzene, the pressure is reduced and the residue is fractionally distilled. There is obtained

29–32 g. of unreacted methyl *p*-ethylbenzoate (b.p. 118–121°/16 mm.), and 43–45 g. (40–42% conversion and 60% yield) of methyl *p*-acetylbenzoate; b.p. 149–150°/7 mm. (Notes 10 and 11). The high-boiling residue weighs 13–18 g. The crude methyl *p*-acetylbenzoate can be purified by crystallization from the minimum amount of 1:1 benzene-commercial hexane required for solution with a recovery of 82–85%, collected in two crops; m.p. 92–95°.

2. Notes

1. A Dean and Stark trap ² modified to provide for continuous return of the heavier organic layer is most convenient. Such a trap can be constructed like a small Wehrli extractor.³

2. Methyl *p*-ethylbenzoate was prepared from ethylbenzene (1 kg.), which was converted into *p*-ethylacetophenone by adding aluminum chloride (792 g.), followed by acetyl chloride (462 g.), which was added with stirring at 0–5° over a period of 3 hours. The mixture was stirred for 1 hour longer, allowed to stand overnight, and washed with iced dilute hydrochloric acid. The ethylbenzene was removed by distillation, and the crude product was oxidized to *p*-ethylbenzoic acid with alkaline hypochlorite.⁴ Recrystallization of the crude acid from 95% ethanol yielded 350 g. (41%) of the pure acid; m.p. 110–112°. Esterification with methanol in the presence of hydrogen chloride ⁴ yielded methyl *p*-ethylbenzoate (77–79%).

3. A T-tube in the connection between the top of the condenser and the water aspirator is attached to a Bunsen burner. The needle valve of the burner serves as a bleed control valve, regulating the amount of air drawn through the reaction mixture.

4. An oil bath can be used.

5. The air stream should be introduced as rapidly as possible, preferably at a rate which will just permit return of the liquid from the coil condenser. It is equally satisfactory to force air through the mixture from a cylinder or compressed-air line if the air is clean and free from oil. Use of a rapid stream of air and vigorous stirring prevents the catalyst from settling.

6. Removal of the water should be as complete as possible, in order to prevent coagulation of the catalyst, which retards the oxidation.

7. The benzene serves to keep the methyl *p*-acetylbenzoate in solution. If crystallization occurs, the mixture should be warmed to dissolve the ester before filtration.

8. The catalyst should be removed completely, because distillation of the product in the presence of small amounts of the catalyst results in some decomposition with a corresponding lowering of the yield. Use of a filter aid such as Super-Cel aids in separating the catalyst.

9. The submitters used a 120-cm. Vigreux column in distilling the benzene and a 60-cm. Vigreux column in fractionating the product. The checkers used a Widmer column with a 17-cm. spiral for the entire distillation.

10. Cooling water should not be circulated through the condenser during distillation of the product, because the methyl *p*-acetylbenzoate tends to crystallize in the condenser.

11. The submitters have obtained similar yields (40–54% conversion and 60–66% yield) in oxidations on 10 times this scale.

3. Methods of Preparation

Methyl *p*-acetylbenzoate has been prepared by the esterification of *p*-acetylbenzoic acid with methanol in the presence of hydrogen chloride,⁵ by the hydrogenation of methyl *p*-trichloroacetylbenzoate in the presence of a palladium on calcium carbonate catalyst,⁶ and by the air oxidation of methyl *p*-ethylbenzoate.⁴

¹ Monsanto Chemical Company, Dayton, Ohio.

² Dean and Stark, *Ind. Eng. Chem.*, **12**, 486 (1920).

³ Wehrli, *Helv. Chim. Acta*, **20**, 927 (1937).

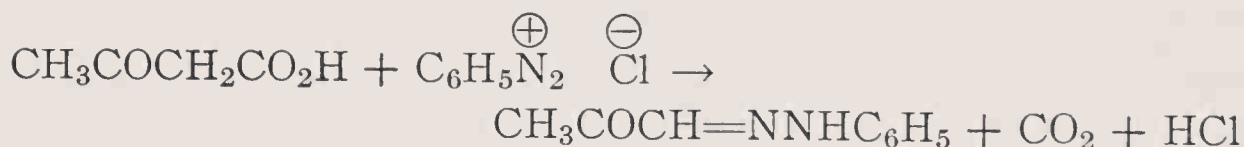
⁴ Emerson, Heyd, Lucas, Chapin, Owens, and Shortridge, *J. Am. Chem. Soc.*, **68**, 674 (1946).

⁵ Meyer, *Ann.*, **219**, 234 (1883).

⁶ Feist, *Ber.*, **67**, 938 (1934).

METHYLGLYOXAL- ω -PHENYLHYDRAZONE

(Pyruvaldehyde, 1-phenylhydrazone)



Submitted by GEORGE A. REYNOLDS and J. A. VANALLAN.¹

Checked by T. L. CAIRNS and C. T. HANDY.

1. Procedure

In a 4-l. beaker equipped with a mechanical stirrer is placed a solution of 30 g. (0.535 mole) of potassium hydroxide in 1120 ml. of water. To the solution is added, with stirring, 65 g. (67 ml., 0.5 mole) of ethyl acetoacetate (Note 1). The mixture is allowed to stand at room temperature for 24 hours.

Forty-seven grams (48 ml., 0.5 mole) of aniline is dissolved in 200 ml. of aqueous hydrochloric acid (prepared from equal volumes of concentrated acid and water) in a 2-l. beaker. The beaker is equipped with a mechanical stirrer and immersed in an ice-salt bath. After the solution has cooled to $\pm 5^\circ$, 36 g. (0.52 mole) of sodium nitrite dissolved in 1 l. of water is added slowly, with stirring, from a separatory funnel. The tip of the stem of the separatory funnel should dip well below the surface of the liquid. The rate of addition is adjusted to maintain the temperature below 10° . A drop of the reaction mixture is tested from time to time with starch-iodide paper (Note 2). The sodium nitrite solution is added until nitrous acid persists in the solution during a 5-minute interval.

The solution of potassium acetoacetate is cooled to 0° , and 45 ml. of concentrated hydrochloric acid in 150 ml. of ice water is added slowly with stirring (Note 3). The diazonium salt solution is then added over a period of 20 minutes, and the

mixture is made basic by the addition of 82 g. of sodium acetate dissolved in 300 ml. of water (Note 4). The temperature of the reaction mixture is raised slowly to 50° and maintained at this value for 2 hours; the solid that separates is collected on a filter and dried. The yield of crude product is 72–77 g. (89–95%). Purification can be effected by recrystallization from 200 ml. of toluene. The purified product weighs 59–66 g. (73–82%) (Notes 5 and 6); m.p. 148–150°.

2. Notes

1. Commercial ethyl acetoacetate was used.
2. The test is made by diluting the test drop on a watch glass with about 1 ml. of water and then placing a drop of this solution on the starch-iodide paper.
3. The solution is neutralized slowly in order to keep it cold so that the acetoacetic acid will not be decomposed.
4. The reaction proceeds much more rapidly in basic solution.
5. An additional 4–6 g. of product separates slowly from the filtrate.
6. This general procedure is effective for the preparation of many types of phenylhydrazones. For example, a substituted diazo compound can be employed.² Alkylated acetoacetic esters³ and ethyl benzoylacetate⁴ may be used. For the higher homologs, the α -formyl derivatives of ketones may be used in place of ethyl acetoacetate.^{5,6} Ethyl pyridylacetates may also be substituted for ethyl acetoacetate.⁷ The products in these cases are the phenylhydrazones of 2-acylpyridines.

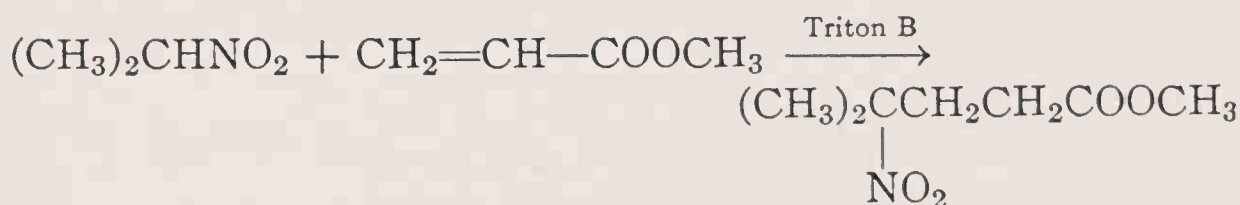
3. Methods of Preparation

The procedure described is essentially that of Japp and Klingemann.³ Methylglyoxal- ω -phenylhydrazone may also be prepared by heating phenylazoacetoacetic acid at 170–180°^{8,9} or by warming ethyl phenylazoacetoacetate with a solution of sodium hydroxide in dilute ethanol.^{8,9}

- ¹ Eastman Kodak Company, Rochester, New York.
² Stierlin, *Ber.*, **21**, 2124 (1888).
³ Japp and Klingemann, *Ann.*, **247**, 218 (1888).
⁴ Bamberger and Schmidt, *Ber.*, **34**, 2009 (1901).
⁵ Benary, *Ber.*, **59**, 2198 (1926).
⁶ Benary, Meyer, and Charisius, *Ber.*, **59**, 108, 600 (1926).
⁷ Frank and Phillips, *J. Am. Chem. Soc.*, **71**, 2804 (1949).
⁸ Richter and Munzer, *Ber.*, **17**, 1928 (1884).
⁹ Japp and Klingemann, *Ann.*, **247**, 198 (1888).

METHYL γ -METHYL- γ -NITROVALERATE

(Isocaproic acid, γ -nitro, methyl ester)



Submitted by R. B. MOFFETT.¹

Checked by N. J. LEONARD and B. L. RYDER.

1. Procedure

A 500-ml. three-necked flask is fitted with a stirrer, a dropping funnel, and a thermometer placed so that the bulb is near the bottom of the flask. In the flask are placed 89 g. (1 mole) of 2-nitropropane (Note 1), 50 ml. of dioxane, and 10 ml. of a 40% aqueous solution of benzyltrimethylammonium hydroxide (Triton B) (Note 2), and the contents of the flask are warmed to 70°. Eighty-six grams (1 mole) of redistilled methyl acrylate (Note 3) is added, with stirring, during 15 minutes. The temperature rises to about 100° during the addition and then drops to about 85°. The mixture is stirred and heated on a steam bath for 4 hours. After cooling, the contents of the flask are acidified with dilute hydrochloric acid and extracted with ether. The ether layer is washed twice with water, then with approximately 50 ml. of 0.1% sodium bicarbonate solution, and finally again with water. After the ethereal solution has been dried

over anhydrous sodium sulfate, the drying agent is separated, the solvent is removed by distillation, and the product is distilled through a short fractionating column. A nearly colorless oil is obtained in a yield of 140–151 g. (80–86%); b.p. 79°/1 mm.; n_D^{20} 1.4408.

2. Notes

1. 2-Nitropropane from Commercial Solvents Corporation, Terre Haute, Indiana, was redistilled before use.

2. Available from Commercial Solvents Corporation or Rohm and Haas Company, Philadelphia, Pennsylvania.

3. Although the submitter knows of no case of an explosion with this type of nitro compound, it is recommended that adequate safety shields be employed during both the reaction and the distillation.

3. Methods of Preparation

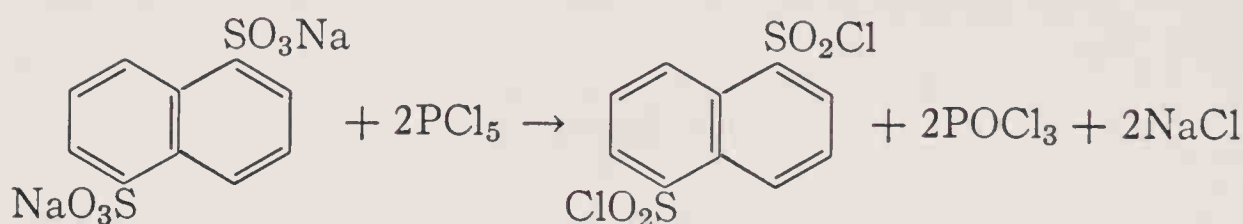
Methyl γ -methyl- γ -nitrovalerate has been prepared by the Michael-type condensation of 2-nitropropane with methyl acrylate in the presence of a quaternary ammonium hydroxide² or triethylamine.³

¹ The Upjohn Company, Kalamazoo, Michigan.

² Bruson, U. S. pat. 2,342,119 and 2,390,918 [*C. A.*, **38**, 4619 (1944)].

³ Kloetzel, *J. Am. Chem. Soc.*, **70**, 3571 (1948).

NAPHTHALENE-1,5-DISULFONYL CHLORIDE

Submitted by P. D. CAESAR.¹

Checked by R. T. ARNOLD and GEORGE P. SCOTT.

1. Procedure

In a 1-l. round-bottomed flask is placed a mixture of 204.3 g. (1 mole) of finely divided phosphorus pentachloride and 132.8 g. (0.4 mole) of the disodium salt of naphthalene-1,5-disulfonic acid which has been dried previously at 140° for 48 hours (Note 1). The flask is provided with an air condenser which is fitted at the top with a calcium chloride drying tube. It is then placed in an oil bath which is heated to 110° , and the mixture is maintained at that temperature for 1 hour. The condenser is removed for brief intervals now and then during the heating period, and the reactants are stirred by means of a glass rod. At the end of the heating period, the product is a thick paste.

The flask and contents are placed on a steam cone and heated for 2 hours under vacuum (furnished by a water aspirator) (Note 2) in order to remove the phosphorus oxychloride formed in this process as well as most of the unreacted phosphorus pentachloride. The dry cake is pulverized in a mortar and transferred to a 4-l. beaker. To this is added 750 ml. of distilled water and 2 l. of chloroform. The mixture is placed on a steam bath, heated to boiling, and stirred vigorously until nearly all the solid dissolves. By means of a separatory funnel the layers are separated while still hot. The chloroform solution is again heated to boiling and filtered through a large fluted filter into an Erlenmeyer flask.

After sufficient chloroform has been evaporated to give a solution volume approximating 250 ml., the solution is cooled in an ice bath and the crystalline product collected on a filter. By further concentration of the mother liquor, an additional quantity of naphthalene-1,5-disulfonyl chloride is obtained. A total yield of 85–115 g. (65–88%) of recrystallized material results; m.p. 181–183°.

2. Notes

1. The powdered solids should be thoroughly mixed before heating. This may be done by inserting a rubber stopper into the neck of the reaction flask and shaking vigorously for about 2 minutes. However, an appreciable pressure develops in the flask and care must be taken in removing the stopper.

2. The reaction flask should be connected to the receiver by a tube of large bore and equipped, preferably, with ground-glass fittings. Two traps between the receiver and the aspirator are desirable to assure no contact between the phosphorus chlorides and water.

3. Methods of Preparation

Naphthalene-1,5-disulfonyl chloride has been prepared by the reaction of naphthalene with chlorosulfonic acid.^{2, 3, 4, 5} However, the yields are generally poor and the conditions difficult to reproduce.

¹ Socony-Vacuum Oil Company, Paulsboro, New Jersey.

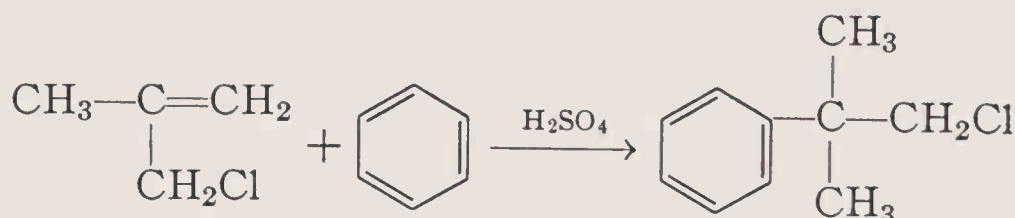
² Armstrong, *J. Chem. Soc.*, **24**, 173 (1871).

³ Armstrong, *Ber.*, **15**, 204 (1882).

⁴ Corbellini, *Giorn. chim. ind. applicata*, **9**, 118 (1927) [*C. A.*, **22**, 2938 (1928)].

⁵ Pollak, Heimberg-Krauss, Katscher, and Lustig, *Monatsh.*, **55**, 358 (1930).

NEOPHYL CHLORIDE

[Benzene (chloro-*tert*-butyl)-]Submitted by W. T. SMITH, JR., and J. T. SELLAS.¹

Checked by N. J. LEONARD and R. O. KERR.

1. Procedure

In a 2-l. three-necked flask equipped with a mechanical stirrer, thermometer, and dropping funnel are placed 500 g. (570 ml., 6.4 moles) of benzene (Note 1) and 34.6 g. (18.8 ml.) of concentrated sulfuric acid (sp. gr. 1.84). The resultant mixture is brought to 20°. To this is added dropwise 201 g. (217 ml., 2.22 moles) of methallyl chloride (Note 2) over a period of 12 hours, during which time vigorous stirring is maintained and the temperature is kept at 20° with the aid of a water bath. The mixture, which becomes an amber color, is stirred for an additional 12 hours.

The reaction mixture is then transferred to a 1-l. separatory funnel, and the sulfuric acid layer is removed. The remaining benzene solution is then washed with four 200-ml. portions of distilled water (Note 3). In this step the amber color disappears and the liquid becomes colorless. The benzene solution is dried with anhydrous sodium sulfate and transferred to a 1-l. distilling flask. The benzene is removed by distillation under a pressure of about 45 mm. The liquid residue is poured into a 500-ml. flask and distilled through a 40-cm. Vigreux column under reduced pressure. The yield of neophyl chloride boiling at 97–98°/10 mm. is 262–275 g. (70–73%) (Notes 4 and 5); n_D^{20} 1.5250.

2. Notes

1. The benzene is purified by washing with three 80-ml. portions of concentrated sulfuric acid and then drying with anhydrous sodium sulfate. It is used directly after removal of the sodium sulfate by filtration.

2. The methallyl chloride used was a redistilled commercial sample and had the following properties: b.p. 71–72°/760 mm., n_D^{20} 1.4274, d_4^{20} 0.918.

3. To ensure good results it is necessary to remove all of the sulfuric acid by washing the mixture thoroughly with water. The final washing should be neutral to litmus.

4. If the residue in the distilling flask is dissolved in ether, treated with activated carbon, and evaporated to dryness, the solid so obtained can be recrystallized from about 25 ml. of 95% ethanol to give 10 g. (2.7%) of *p*-di-(chloro-*tert*-butyl)-benzene; m.p. 54.5–55.0°.

5. In a run in which the temperature was kept at 10–15° during the addition of methallyl chloride, the methallyl chloride was added over a period of 1 hour. Stirring was continued for 1 hour, and the reaction mixture was worked up as described above to give a 53% yield.

3. Methods of Preparation

(Chloro-*tert*-butyl)-benzene has been prepared by the direct chlorination of *tert*-butylbenzene in the presence of strong light;² by chlorination of *tert*-butylbenzene with sulfuryl chloride in the presence of benzoyl peroxide;³ by the action of thionyl chloride on the corresponding alcohol;⁴ and by the hydrogen fluoride-catalyzed alkylation of benzene with methallyl chloride.⁵ The sulfuric acid-catalyzed alkylation described here is based on the procedure of Whitmore, Weisgerber, and Shabica.⁶ A variation using a shorter reaction time has also been described.⁷

¹ The State University of Iowa, Iowa City, Iowa.

² Truce, McBee, and Alfieri, *J. Am. Chem. Soc.*, **71**, 752 (1949).

³ Kharasch and Brown, *J. Am. Chem. Soc.*, **61**, 2147 (1939).

⁴ Haller and Ramart, *Compt. rend.*, **174**, 1211 (1922).

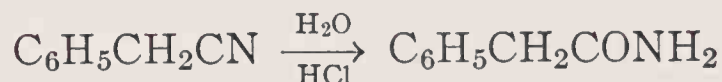
⁵ Calcott, Tinker, and Weinmayr, *J. Am. Chem. Soc.*, **61**, 1010 (1939).

⁶ Whitmore, Weisgerber, and Shabica, *J. Am. Chem. Soc.*, **65**, 1469 (1943).

⁷ Schmerling and Ipatieff, *J. Am. Chem. Soc.*, **67**, 1862 (1945).

PHENYLACETAMIDE

(Acetamide, α -phenyl-)



Submitted by WILHELM WENNER.¹

Checked by WILLIAM S. JOHNSON and ROBERT E. IRELAND.

1. Procedure

In a 3-l. three-necked round-bottomed flask equipped with glass joints are placed 200 g. (1.71 moles) of benzyl cyanide (Note 1) and 800 ml. of 35% hydrochloric acid (Note 2). The flask is fitted with a reflux condenser, a thermometer, and an efficient mechanical stirrer (Note 3). At a bath temperature of about 40° (Note 4) the mixture is stirred vigorously. Within a period of 20–40 minutes the benzyl cyanide goes into solution (Note 3). During this time, the temperature of the reaction mixture rises about 10° above that of the bath. The homogeneous solution is kept in the bath with, or without, stirring for an additional 20–30 minutes (Note 5). The warm water in the bath is replaced by tap water at about 15–20°, and the thermometer is replaced by a dropping funnel from which 800 ml. of cold distilled water is added with stirring (Note 6). After the addition of about 100–150 ml., crystals begin to separate. When the total amount of water has been added, the mixture is cooled externally with ice water for about 30 minutes (Note 7). The cooled mixture is filtered by suction. Crude phenylacetamide remains on the filter and is washed with two 100-ml. portions of water. The crystals are then dried at 50–80°. The yield of crude phenylacetamide is 190–200 g. (82–86%). It is sufficiently pure for most purposes although it contains traces

of phenylacetic acid. If pure phenylacetamide is desired, the crude, wet solid is stirred for about 30 minutes with 500 ml. of a 10% solution of sodium carbonate, collected on a suction funnel, washed with two 100-ml. portions of cold water, and dried. The yield of this product is 180–190 g. (78–82%); m.p. 154–155° (Notes 8 and 9).

2. Notes

1. The quality of the benzyl cyanide markedly affects the yields. Material prepared according to directions given previously² is satisfactory. Several commercially available grades were also found to be usable without distillation.

2. The hydrochloric acid must be of at least 30% strength.

3. Efficient stirring is of prime importance for satisfactory reaction, because intimate mixing of the heterogeneous mixture is necessary. The rate of dissolution of the nitrile depends on the efficiency of the stirring.

4. The reaction proceeds slowly at lower temperatures. Temperatures above 50° are not recommended because of the high volatility of hydrochloric acid.

5. This additional warming ensures complete reaction of some dissolved benzyl cyanide. The phenylacetamide is not readily hydrolyzed under these conditions.

6. The rate of addition is not critical.

7. If phenylacetic acid is desired, the suspension of phenylacetamide is refluxed with stirring and the phenylacetamide redissolves. After about 30 minutes, the mixture becomes turbid and the product begins to separate as an oil. After 6 hours the mixture is cooled, first with tap water and then by an ice-water bath. When the temperature has dropped to about 40–50°, the phenylacetic acid crystallizes. After cooling at 0° for about 4 hours (the acid is rather soluble in warm water), the mixture is filtered by suction. The crude, colorless phenylacetic acid is washed with two 100-ml. portions of cold water and dried in a desiccator. The yield of crude acid is 180–195 g. (77.5–84%). It melts at 66–70° and is sufficiently pure for most

purposes. The mother liquor on extraction with two 150-ml. portions of benzene and evaporation yields an additional 3–5 g. of acid. To prepare the pure acid, vacuum distillation (as described by Adams and Thal³) is simpler and gives higher yields than recrystallization from ligroin.

8. Further purification is effected by recrystallization from 95% ethanol or benzene, yielding the pure compound of m.p. 156°.

9. The following arylacetamides have been prepared from the corresponding nitriles by the same method in the indicated yields: ⁴ *p*-methylphenylacetamide (70%), *p*-isopropylphenylacetamide (90%), 1-naphthylacetamide (54%), 5,6,7,8-tetrahydro-2-naphthylacetamide (90%), *p*-methoxyphenylacetamide (76%), 3,4-dimethoxyphenylacetamide (82%), and 2,3-dimethoxyphenylacetamide (91%). Only in the cases of the alkoxy-substituted nitriles are the resulting amides soluble in the reaction mixture; the other nitriles do not dissolve completely at any time during the reaction.

3. Methods of Preparation

Phenylacetamide has been obtained by a wide variety of reactions: from benzyl cyanide with water at 250–260°; ⁵ from benzyl cyanide with water and cadmium oxide at 240°; ⁶ from benzyl cyanide with sulfuric acid; ^{7,8} by saturation of an acetone solution of benzyl cyanide with potassium hydrosulfide; ⁹ from benzyl cyanide with sodium peroxide; ¹⁰ by electrolytic reduction of benzyl cyanide in sodium hydroxide; ¹¹ from ethyl phenylacetate with alcoholic ¹² or aqueous ¹³ ammonia; from phenylacetic acid with ammonium acetate ¹⁴ or urea; ¹⁵ from diazoacetophenone with ammoniacal silver solution; ¹⁶ from phenylacetic acid imino ether hydrochloride and water; ¹⁷ from acetophenone with ammonium polysulfide at 215°; ¹⁸ from benzoic acid; ¹⁹ and by heating the ammonium salt of phenylacetic acid.²⁰

The literature on the preparation of phenylacetic acid is reviewed in an earlier volume of this series.³

The present method is that of Wenner²¹ and is applicable to other arylacetoneitriles.⁴

Sodium Nitromalonaldehyde Monohydrate

WARNING

The sodium salt of nitromalonaldehyde [*Org. Syntheses*, **32**, 95 (1952)] is impact-sensitive and thermally unstable and should be handled as a potentially explosive material.

Please insert this sheet opposite page 95 of *Org. Syntheses*, **32** (1952).

Sodium Nitromalonaldehyde Monohydrate

WARNING

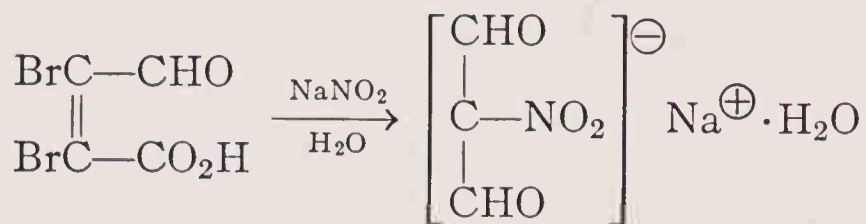
The sodium salt of nitromalonaldehyde [*Org. Syntheses*, **32**, 95 (1952)] is impact-sensitive and thermally unstable and should be handled as a potentially explosive material.

Please insert this sheet opposite page 95 of *Org. Syntheses*, **32** (1952).

- ¹ Hoffmann-La Roche, Inc., Nutley, New Jersey.
- ² *Org. Syntheses* Coll. Vol. **1**, 107 (1941).
- ³ *Org. Syntheses* Coll. Vol. **1**, 436 (1941).
- ⁴ Wenner, *J. Org. Chem.*, **15**, 548 (1950).
- ⁵ Bernthsen, *Ann.*, **184**, 318 (1877).
- ⁶ I. G. Farbenind., Ger. pat. 551,869 [C. A., **26**, 4826 (1932)].
- ⁷ Maxwell, *Ber.*, **12**, 1764 (1879).
- ⁸ Purgotti, *Gazz. chim. ital.*, **20**, 173, 593 (1891).
- ⁹ Weddige, *J. prakt. Chem.*, [2] **7**, 99 (1873).
- ¹⁰ Deinert, *J. prakt. Chem.*, [2] **52**, 432 (1895).
- ¹¹ Ogura, *Mem. Coll. Sci., Kyoto Imp. Univ.*, **12A**, 339 (1929) [C. A., **24**, 2060 (1930)].
- ¹² Fischer and Dilthey, *Ber.*, **35**, 856 (1902).
- ¹³ Meyer, *Monatsh.*, **27**, 34 (1906).
- ¹⁴ Kao and Ma, *J. Chem. Soc.*, **1930**, 2788; **1931**, 443.
- ¹⁵ Das-Gupta, *J. Ind. Chem. Soc.*, **10**, 117 (1933).
- ¹⁶ Wolff, *Ann.*, **394**, 43 (1912).
- ¹⁷ Houben, *Ber.*, **59**, 2878 (1926).
- ¹⁸ Willgerodt and Scholtz, *J. prakt. Chem.*, [2] **81**, 384 (1910).
- ¹⁹ Arndt and Eistert, *Ber.*, **68**, 200 (1935).
- ²⁰ Menschutkin, *Ber.*, **31**, 1429 (1898).
- ²¹ Wenner, U. S. pat. 2,489,348 [C. A., **44**, 2559 (1950)].

SODIUM NITROMALONALDEHYDE MONOHYDRATE

(Malonaldehyde, nitro-, sodium derivative)



Submitted by PAUL E. FANTA.¹

Checked by CLIFF S. HAMILTON and PHILIP J. VANDERHORST.

1. Procedure

In a 2-l. three-necked round-bottomed flask, equipped with a thermometer, a dropping funnel, a mechanical stirrer and a gas vent (Note 1), are placed 258 g. (3.74 moles) of sodium nitrite and 250 ml. of water. The contents of the flask are heated and stirred to dissolve the solid. A solution of 258 g. (1 mole) of mucobromic acid ² in 250 ml. of warm 95% ethanol is placed in

the dropping funnel and added dropwise with constant stirring over a period of 70–80 minutes. A mildly exothermic reaction occurs; the solution in the flask becomes deep red, and gas is evolved. During the addition, the temperature is kept at $54 \pm 1^\circ$ by intermittent application of an ice bath to the flask (Note 2). The mixture is stirred for an additional 10 minutes at $54 \pm 1^\circ$. While being stirred continuously, it is then cooled to $0-5^\circ$ by application of an ice bath. The fine, yellow precipitate is collected on a previously chilled Büchner funnel.

The slightly moist cake of crude product is transferred to a 1-l. flask and heated to boiling with a mixture of 400 ml. of 95% ethanol and 100 ml. of water. The hot solution is filtered to remove a fine yellow solid, and the clear red filtrate is cooled to $0-5^\circ$. The recrystallized product is collected on a Büchner funnel and dried in air at room temperature. The yield is 57–65 g. (36–41%) of pink or tan needles of sodium nitromalonaldehyde monohydrate (Note 3).

2. Notes

1. The gases evolved are slightly irritating; they should be vented to a trap,³ or the apparatus should be set up in a hood.

2. The yield is not increased and a darker, less pure product is obtained if the reaction is run at a higher temperature or for a longer time.

3. The checkers found the product to be quite pure. An almost quantitative yield of 2-amino-5-nitropyrimidine was obtained by reaction of the product with guanidine.

3. Methods of Preparation

The above procedure is a modification of the method of Hill and Torrey,⁴ which was also studied by Johnson.⁵

¹ Illinois Institute of Technology, Chicago, Illinois.

² *Org. Syntheses*, **27**, 60 (1947).

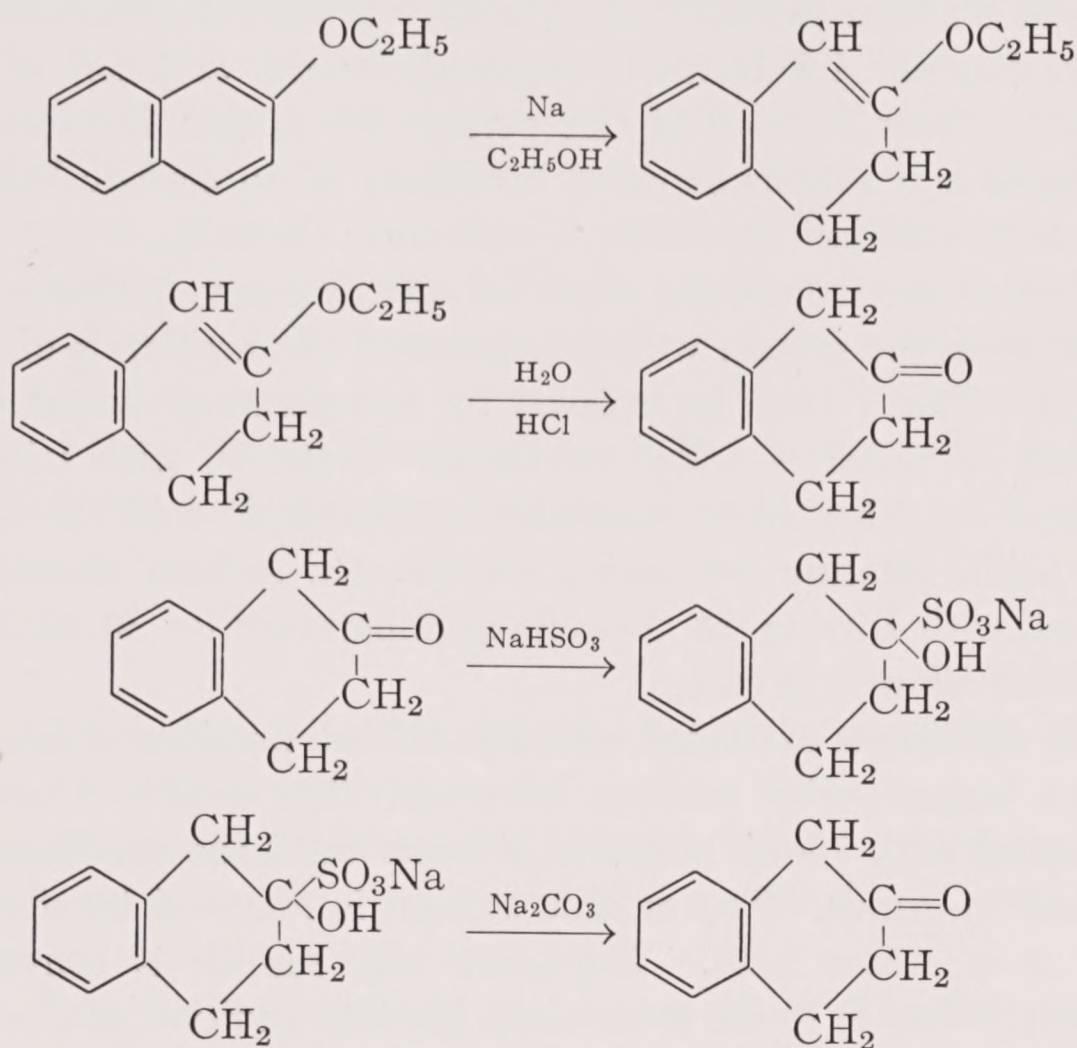
³ *Org. Syntheses Coll. Vol. 2*, 4 (1943).

⁴ Hill and Torrey, *Am. Chem. J.*, **22**, 89 (1899).

⁵ Johnson, P. B. Report 31092, "Preparation of Nitro Compounds" (1941) [*U. S. Bibliog. of Scientific and Industrial Reports*, **2**, 785 (1946)].

β -TETRALONE

(3,4-Dihydro-2(1H)-naphthalenone)



Submitted by M. D. SOFFER, M. P. BELLIS, HILDA E. GELLERSON,
and ROBERTA A. STEWART.¹

Checked by N. J. LEONARD and R. C. FOX.

1. Procedure

A. *Reduction and hydrolysis.* A solution of 129 g. (0.75 mole) of β -naphthyl ethyl ether in 1.5 l. of 95% ethanol is prepared in a 5-l. three-necked flask fitted with a mechanical stirrer, a bulb condenser topped by a Friedrichs condenser, and a Y-tube to allow for the introduction of nitrogen and sodium. The apparatus is flushed thoroughly with nitrogen, the nitrogen flow is reduced, and 225 g. (9.8 gram atoms) of sodium is added in small portions (Note 1), with efficient stirring, at a rate suffi-

cient to maintain vigorous boiling. The hydrogen liberated passes through the condensers and a delivery tube into a hood or directly out a window. When approximately two-thirds of the sodium has been introduced, an additional 375 ml. of 95% ethanol is added to reduce the viscosity of the reaction mixture. Approximately 1.5 hours is required for the addition of the sodium. Near the end of this period, the rate of the reaction decreases and heat is supplied by means of an electric heating mantle to maintain the reflux temperature (Note 2).

After all the sodium has dissolved, the hydrogen is thoroughly swept from the system with nitrogen and the heating is discontinued. The Y-tube is replaced by a separatory funnel, and 750 ml. of water is added cautiously (Note 3), with stirring, followed by 1.5 l. of concentrated hydrochloric acid (Note 3). The acidic mixture containing precipitated sodium chloride is heated, with stirring, at the reflux temperature for 30 minutes, and then allowed to cool.

The mixture is extracted with ten 175-ml. portions of benzene or 1:1 benzene-ether mixture (Note 4). The combined extract is washed with 75-ml. portions of water until the washings are neutral to litmus. The organic solvent is removed by distillation on a steam bath. The crude oily residue is converted directly (Note 5) to the β -tetralone bisulfite addition product.

B. *Bisulfite addition product of β -tetralone.* To a solution of 325 g. (3.12 moles) of sodium bisulfite (commercial purified grade) in 565 ml. of water is added 175 ml. of 95% ethanol. The mixture is allowed to stand overnight, and the precipitated sodium bisulfite is removed by filtration. The filtrate is added to the crude β -tetralone, and the mixture is shaken vigorously. Within a few minutes the addition product separates as a voluminous precipitate. The mixture is kept cold for several hours, shaken periodically, and then filtered with the aid of suction. The precipitate is washed well, first with 125 ml. of 95% ethanol, then four times with 125-ml. portions of ether (Note 6). The colorless addition product is air-dried (Note 5) and is stored in air-tight containers. The yield is 113–131 g. (60–70% based on β -naphthyl ethyl ether) (Note 7).

C. *Regeneration of β -tetralone.* Fifty grams (0.20 mole) of β -tetralone bisulfite addition product is suspended in 250 ml. of water, and 75 g. (0.6 mole) of sodium carbonate monohydrate is added. At this point the *pH* of the solution is approximately 10. The mixture is extracted with five 100-ml. portions of ether (Note 8). The combined extract is washed with 100 ml. of 10% hydrochloric acid, then with 100-ml. portions of water until the washings are neutral to litmus, and is dried over anhydrous magnesium sulfate. The ether is removed by distillation, and the residue is distilled from a Claisen flask under reduced pressure, preferably in a nitrogen atmosphere. The pure β -tetralone is obtained as a colorless distillate; b.p. 70–71°/0.25 mm. (92–94°/1.8 mm., 114–116°/4.5 mm.); n_D^{20} 1.5594. The yield is 17–21 g. (40–50% based on β -naphthyl ethyl ether).

2. Notes

1. The sodium is cut into pieces about 2 in. by 0.5 in. by 0.5 in. and is kept under benzene until used.

2. The concentrated sodium ethoxide solution must be kept hot throughout the process; otherwise a voluminous precipitate separates and the mixture congeals.

3. Both the hydrolysis of the sodium ethoxide and the subsequent neutralization are very exothermic. The water and the acid may be added fast enough to maintain vigorous refluxing, but care must be exercised to keep the reaction under control. When the neutralization is complete, the refluxing subsides, and at this point the excess hydrochloric acid may be added rapidly.

4. Ether is somewhat miscible with the reaction mixture, but the benzene-ether mixture, or benzene alone, is satisfactory.

5. In this step the β -tetralone is separated from starting material and other neutral substances in the reaction mixture. β -Tetralone is sensitive to air oxidation; therefore it should not be stored in the free state. The bisulfite addition product is stable, and the dry material can be stored indefinitely without deterioration.

6. In order to obtain a product of high quality, the washing must be thorough. This is accomplished best by suspending the precipitate in the wash solvent and mixing well before filtering.

7. The yield of the bisulfite addition product is subject to variation owing to coprecipitation of sodium bisulfite.

8. The ether extract and the water layer may be tested for the presence of β -tetralone or the bisulfite addition product by the tetralone blue test.

Tetralone blue test. A few drops of the organic solvent layer or the aqueous phase is shaken in a test tube with 2 ml. of 95% ethanol, and 10 drops of 25% sodium hydroxide solution is poured down the side of the tube. In the presence of air a deep blue color appears at the interface within 1 minute.

3. Methods of Preparation

β -Tetralone has been prepared by a variety of methods, but the only practical procedures are relatively recent ones involving reduction of β -naphthyl methyl ether with sodium and alcohol² or with sodium and liquid ammonia,³ high-pressure catalytic hydrogenation of β -naphthol,⁴ or catalytic oxidation of 2-tetralol by hydrogen transfer with ethylene.⁵

The procedure described here is an adaptation⁶ of the method of Cornforth, Cornforth, and Robinson.²

¹ Smith College, Northampton, Massachusetts.

² Cornforth, Cornforth, and Robinson, *J. Chem. Soc.*, **1942**, 689.

³ Birch, *J. Chem. Soc.*, **1944**, 430.

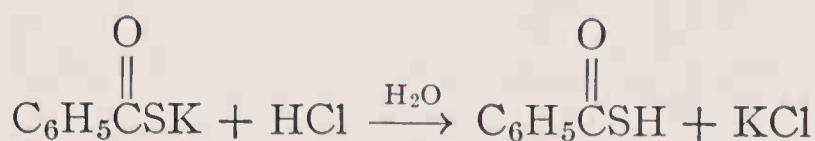
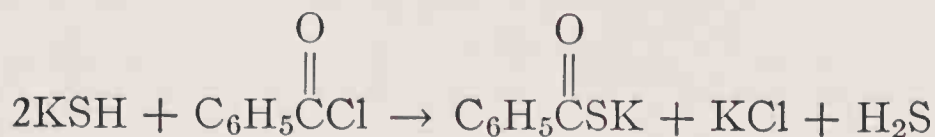
⁴ Stork and Foreman, *J. Am. Chem. Soc.*, **68**, 2172 (1946).

⁵ Adkins, Rossow, and Carnahan, *J. Am. Chem. Soc.*, **70**, 4247 (1948).

⁶ Soffer, Stewart, Cavagnol, Gellerson, and Bowler, *J. Am. Chem. Soc.*, **72**, 3704 (1950).

THIOBENZOIC ACID

(Benzoic acid, thio)

Submitted by PAUL NOBLE, JR., and D. S. TARBELL.¹

Checked by WILLIAM S. JOHNSON and ROBERT A. KLOSS.

1. Procedure

A solution of 200 g. (3 moles) of potassium hydroxide (85%) pellets in 800 ml. of 90% ethanol (Note 1) is prepared with mechanical stirring in a 2-l. three-necked round-bottomed flask. The flask is fitted with a 500-ml. dropping funnel and a gas inlet tube extending to the bottom of the flask, and hydrogen sulfide is passed in through the inlet tube with stirring and cooling until the solution is saturated and does not give an alkaline reaction with phenolphthalein (Notes 2 and 3). The mixture is further cooled to 10–15° by means of an ice bath, and 200 g. (1.41 moles) of freshly distilled benzoyl chloride (Note 4) is introduced dropwise over a period of about 90 minutes with stirring while the temperature is kept below 15°. After the addition of the benzoyl chloride is completed, the reaction mixture is stirred for an additional hour. The potassium chloride which precipitates during the addition is separated quickly by filtration through a Büchner funnel and is washed with about 200 ml. of 95% ethanol. The filtrate is placed in a 2-l. round-bottomed flask fitted with a condenser arranged for distillation and evaporated to dryness under reduced pressure on a steam bath (Note 5). The solid residue, consisting mainly of potassium thiobenzoate, is dissolved in about 700 ml. of cold water (Note 6), and the solution is filtered

if considerable insoluble material is present (Note 4). The alkaline solution is extracted with 500 ml. of benzene in order to remove any neutral material. The aqueous layer is then acidified with cold 6 *N* hydrochloric acid (Note 6) and extracted with two 500-ml. portions of peroxide-free ether (Note 7). The ether layer is washed with several portions of cold water and dried over anhydrous sodium sulfate. The ether is evaporated under reduced pressure on a steam bath (Note 5), and the residue is fractionated immediately through a short (15–20 cm.) Vigreux column at reduced pressure, dry nitrogen being admitted through the capillary (Note 8). After a very small fore-run, the yellow-orange thiobenzoic acid distils at 85–87°/10 mm. (95–97°/15 mm.); yield 120–150 g. (61–76%); n_D^{20} 1.6027. Upon refractionation, the light-yellow thiobenzoic acid, as determined by titration with standard base or alcoholic iodine, is about 99.5% pure; n_D^{20} 1.6030.

2. Notes

1. No improvement in yield was observed by substitution of absolute ethanol. The 90% is preferable to 95% ethanol, because a much smaller volume is required to dissolve the potassium hydroxide.

2. The preparation should be conducted in a well-ventilated hood or provision should be made for an exhaust tube and attachment to a gas-absorption trap.

3. The gas inlet tube should be of moderately large diameter to prevent becoming plugged with crystals during the saturation with hydrogen sulfide.

4. The use of benzoyl chloride which has not been redistilled lowers the yield by 20–30%. The use of a molar equivalent of benzoyl chloride leads to the formation of considerable benzal *bis*-thiobenzoate, $C_6H_5CH(SCOC_6H_5)_2$, which has been isolated previously as a product from the action of benzoyl chloride on potassium sulfide in ethanol.²

5. In order to prevent oxidation, it is inadvisable to allow the solution to stand for any appreciable time up to this point. The evaporation should be carried out without the use of a

capillary. The checkers found it convenient to employ mechanical stirring (rubber-sealed stirrer) during the reduced-pressure distillation in order to prevent bumping.

6. If the temperature is allowed to rise, considerable oxidation may occur.

7. Suitable peroxide-free ether is prepared by washing ether with an equal volume of a dilute, weakly acidic solution of ferrous sulfate.

8. It is necessary to fractionate as rapidly as possible in order to prevent oxidation to the disulfide, which occurs almost completely even in the presence of nitrogen if the column is too long or if the distillation is carried out too slowly. Oil-pumped nitrogen is dried through an absorption tower containing soda lime and calcium chloride before passing to the distillation apparatus. The column should be vacuum jacketed or provided with a heated jacket.

3. Methods of Preparation

The method described is adapted from the procedures of Kym³ and Engelhardt, Latschinoff, and Malyscheff.⁴ Thio-benzoic acid has been prepared by the reaction of benzoyl chloride with potassium sulfide,⁴ hydrogen sulfide in pyridine,^{5,6} and magnesium bromide hydrosulfide.⁷ It is formed from dibenzoyl disulfide with potassium hydrosulfide,⁴ potassium hydroxide,^{4,8} and ammonia.⁹ It is also formed from dibenzoyl sulfide, from phenyl benzoate, and from benzoic anhydride with alcoholic potassium hydrosulfide.⁴ It has been obtained from dibenzoyl sulfide and hydrogen sulfide,¹⁰ carbon oxysulfide and phenyl-magnesium bromide,^{11,12} dibenzyl disulfide and sodium ethoxide,¹³ benzyl chloride and sulfur in the presence of potassium hydroxide,¹⁴ and benzylthiosulfuric acid and alkali.^{15,16}

¹ University of Rochester, Rochester, New York.

² Bergmann, *Ber.*, **53**, 981 (1920).

³ Kym, *Ber.*, **32**, 3533 (1899).

⁴ Engelhardt, Latschinoff, and Malyscheff, *Z. Chem.*, **4**, 354 (1868).

⁵ Sunner and Nilson, *Svensk Kem. Tid.*, **54**, 163 (1942).

⁶ Lewis, *J. Chem. Soc.*, **1940**, 831.

⁷ Mingoia, *Gazz. chim. ital.*, **55**, 717 (1925).

⁸ Fromm and Schmoldt, *Ber.*, **40**, 2863 (1907).

⁹ Busch and Stern, *Ber.*, **29**, 2150 (1896).

¹⁰ Adkins and Thompson, *J. Am. Chem. Soc.*, **71**, 2244 (1949).

¹¹ Weigert, *Ber.*, **36**, 1010 (1903).

¹² Bloch, *Compt. rend.*, **204**, 1342 (1937).

¹³ Fromm and Forster, *Ann.*, **394**, 338 (1912).

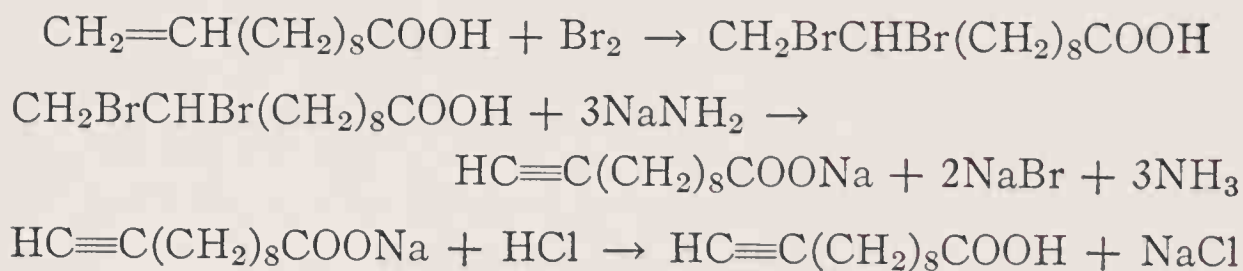
¹⁴ Fromm and de Seixas Palma, *Ber.*, **39**, 3324 (1906).

¹⁵ Price and Twiss, *J. Chem. Soc.*, **93**, 1399 (1908).

¹⁶ Fromm and Erfurt, *Ber.*, **42**, 3818 (1909).

10-UNDECYNOIC ACID

(10-Hendecynoic acid)



Submitted by N. A. KHAN.¹

Checked by T. L. CAIRNS and D. H. SMITH.

1. Procedure

Caution! All reactions involving liquid ammonia must be carried out in an effective hood.

Bromine (approximately 15 ml.) is added dropwise to 50 g. (0.271 mole) of 10-undecenoic acid (Note 1) dissolved in 210 ml. of dry ether with constant stirring while the temperature is maintained below 0° until the color of bromine persists. The excess bromine is then removed by the addition of a few drops of 10-undecenoic acid.

The sodamide for dehydrobromination of dibromohendecanoic acid is prepared according to the method of Khan et al.,² with some modifications (Note 2). A 3-l. three-necked flask is equipped with a stirrer and a Dry Ice-acetone cold finger reflux condenser attached through a drying tube to a trap and a bubbler filled with a saturated ammonia solution. After the con-

denser has been cooled with a mixture of Dry Ice and acetone, 1.5 l. of liquid ammonia is introduced into the flask through an inlet tube. Stirring is started, and 1.2–1.5 g. of ferric chloride (c.p., anhydrous, black) is added to the liquid ammonia in one portion as quickly as possible. Within 20 seconds after this addition, 6 g. of metallic sodium is dropped into the brown solution in two portions in order to convert the iron salt into catalytic iron. When the evolution of hydrogen gas ceases, the remainder of the sodium (total amount, 27.7 g., 1.2 gram atoms) is added in pieces and the solution is stirred for an additional 30 minutes (Note 3).

Finally, the solution of 10,11-dibromohendecanoic acid in absolute ether is added slowly from a separatory funnel to the reaction flask. The reaction mixture is then stirred for 6 hours. After an additional 1 hour (Note 4) of stirring, during which time the cold-finger condenser is removed from the system, an excess of solid ammonium chloride (40 g., 0.74 mole) is introduced slowly into the reaction mixture to destroy excess sodamide. The ammonia is allowed to evaporate, 400–500 ml. of water is added, and the mixture is stirred until all the solid is broken up and dissolved (Note 5).

The water solution containing the sodium salt of the product is acidified with 6 *N* hydrochloric acid and then extracted with three 200-ml. portions of ether. The ethereal extracts are combined, washed with water (until the aqueous phase shows a *pH* in the range 5–6), and then dried over anhydrous sodium sulfate. After removal of the solvent, the red-colored residual oil is fractionally distilled through a packed column (Note 6). The middle portion (26–28 g.) distilling at 124–130°/3 mm. is crystallized twice from petroleum ether (b.p. 30–60°) to obtain white crystals of 10-undecynoic acid. The end fractions also yield some white product after 4–5 crystallizations. A total yield of 19–24 g. (38–49%) is obtained; m.p. 42.5–43°.

2. Notes

1. 10-Undecenoic acid (undecylenic acid, commercial grade) may be obtained from the Eastman Kodak Company. The pure grade acid is also used with good results. However, for general purposes, no difficulty is encountered in preparing 10-undecynoic acid from the commercial grade acid if the final fractionation by vacuum distillation is carried out carefully.

2. The experiences with this particular preparation have led to some changes in the procedure of preparing sodamide. However, for large-scale preparation (larger than that reported here), Khan et al.² and Greenlee and Henne³ have given very specific details of the methods that are to be followed. It is to be noted that the use of a Hershberg stirrer (with a rubber stopper and a powerful high-speed motor) is advantageous.

3. The complete transformation of metallic sodium into sodamide may be checked by the method of Greenlee and Henne.³ When the evolution of hydrogen gas ceases (bubbler), it may be assumed that the above transformation is complete.

4. The checkers observed the yield to be increased somewhat by the less convenient procedure of allowing the ammonia to evaporate slowly for 12–15 hours.

5. More water may be added if needed.

6. The fractionation has also been carried out with better results through a Todd Scientific versatile column.

3. Methods of Preparation

Experiments in the submitter's laboratory have shown that the yield obtained on dehydrobromination of dibromohendecanoic acid with ethanolic potassium hydroxide^{4,5} is very poor, usually lower than 30%. On the other hand, the dehydrobromination with sodamide in liquid ammonia is smooth and very satisfactory. The directions employed here represent a modification of those of Lauer and Gensler.⁶

The submitter gratefully acknowledges the helpful suggestions

of Dr. K. W. Greenlee, Chemistry Department, Ohio State University, and Dr. Theodore Kaskel, Parke Davis and Company, Detroit, Michigan.

¹ Ohio State University, Columbus, Ohio.

² Khan, Deatherage, and Brown, *J. Am. Oil Chemists' Soc.*, **28**, 27 (1951).

³ Greenlee and Henne, *Inorg. Syntheses*, **2**, 128 (1946).

⁴ Krafft, *Ber.*, **29**, 2232 (1896).

⁵ Oskerko, *Ber.*, **70**, 55 (1937).

⁶ Lauer and Gensler, *J. Am. Chem. Soc.*, **67**, 1171 (1945).

SUBJECT INDEX

(This cumulative index comprises material from Volumes 30-32; for previous volumes see Collective Volumes 1 and 2 and Volume 29.)

Names in small capital letters refer to the titles of individual preparations. A number in ordinary bold-face type denotes the volume. A page number in bold-face italics indicates that the detailed preparative directions are given or referred to; entries so treated include principal products and major by-products, special reagents or intermediates (which may or may not be isolated), compounds mentioned in the text or Notes as having been prepared by the method given, and apparatus described in detail or illustrated by a figure. Page numbers in ordinary type indicate pages on which a compound or subject is mentioned in connection with other preparations. For example, Allylbenzene, **31**, 85, **86**, indicates that allylbenzene is mentioned on page 85, and that directions for its preparation are given on page 86, of Volume 31.

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